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LONDON SATURDAY DECEMBER 27 1941

"GROWTH" AND THE DIABETOGENIC ACTION OF ANTERIOR PITUITARY PREPARATIONS

BY

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Joslin (1940) states that about 80% of his adult diabetic patients are, or have been, over weight at the time they come for treatment, and excessive weight is widely recognized as a frequent characteristic of the elderly diabetic patient. White—quoted by Joslin (1940) and by Coggeshall and Root (1940)—finds that at the onset of diabetes a substantial proportion of her diabetic children are above the average height for their age, and many of these show precocious physical development. In discussing these facts Joslin (1940) asks the pertinent question, "In the child growth is vertical, in the adult it is lateral. Is not each type of endocrinal origin?" The results of the experimental investigation described in the present paper indicate, in relation to the evidence already in the literature, that a positive answer might be given to Joslin's question in terms of pancreatic-hypophysial balance.

The first demonstration of the diabetogenic action of anterior pituitary extract in normal animals was made by Evans, Meyer, Simpson, and Reichert (1931-2) under interesting conditions. Two puppies which had been treated daily with a growth-promoting preparation of ox pituitary gland, and had thereby increased to about twice the weight of control animals, were found to be suffering from polyuria and glycosuria. Two treated litter-mates did not develop this diabetic condition. Using the intact adult dog as a test animal, Young (1939) subsequently found that ammonium sulphate fractionation of a crude extract of ox anterior hypophysis resulted in the precipitation of the diabetogenic principle in the pseudoglobulin fraction, in which it was accompanied by the growth-promoting substance (assayed on the adult intact female rat). Other investigators, using partially depancreatized rats as test objects for diabetogenic activity, have also found a similarity in properties between the growth-promoting and diabetogenic substances (Shipley and Long, 1938). When it is recalled that both Evans, for the growth hormone, and Houssay, for the diabetogenic substance, have strongly emphasized the importance of using absolutely fresh glands for the preparation of active extracts, and of carrying out all procedures at low temperatures, it becomes surprising that more cases have not been recorded of the development of a diabetic condition in the puppies in which gigantism has been produced by treatment with growth-promoting pituitary extracts.

A possible explanation lay in the observation that an adult dog effectively treated with diabetogenic extract for some days eventually developed a refractory state, such that the symptoms of diabetes disappeared during a period of continued similar dosage, though they would reappear if the daily dose of extract were suitably increased (Young, 1937, 1938). It was therefore possible that the puppies treated with growth hormone did exhibit a transient response to the putative diabetogenic action of the extract, but subsequently became refractory to this aspect of its action, while retaining sensitivity to its growth-promoting effect. It seemed desirable to investigate this point, using extracts with a diabetogenic action demonstrable in normal adult dogs.

Growth hormone preparations induce retention of nitrogen (Evans, 1941); and Mirsky (1939) has obtained evidence that this nitrogen-retaining action may be mediated, in part at least, by the islets of Langerhans of the pancreas. An investigation was therefore undertaken of the relation between the nitrogen-retaining and pancreotropic actions of anterior pituitary extracts, in permanently diabetic animals in which some islet tissue remained. By pancreotropic activity is meant that action of pituitary extracts which induces a rise in islet tissue and insulin contents of the rat pancreas (Marks and Young, 1940) and thus makes more insulin available for secretion.

Methods

Animals.—Normal adult dogs, normal puppies, and adult dogs which had been rendered permanently diabetic by a short period of treatment with anterior pituitary extract (Young, 1937) were used in the present investigation. They were housed in metabolism cages, and daily collections of urine were made under toluene. The amount of food eaten each day was determined by weighing, and was so adjusted that the adult dogs retained about 75 calories/kg./day. The puppies were given a mixed diet *ad lib.*, consisting of raw horse meat, cooked liver, dog biscuits, and milk, with vitamin concentrates twice weekly. The adult dogs received a diet of raw horse meat and liver. All the animals were weighed daily.

Anterior Pituitary Extracts.—A crude extract of fresh ox pituitary tissue was prepared, from glands brought to the laboratory in a frozen condition, by the method before described (Young, 1938), to which further procedures have now been added. In brief, the method consisted in extraction with saline at *p*H 8.5 in the cold room, followed by spinning on an international centrifuge, clarification in a Sharples supercentrifuge, and Seitz-filtration in the cold room. Bacteriological tests were carried out to ensure that sterility had been obtained. This preparation, which will be referred to as "crude pituitary extract," is highly diabetogenic in normal dogs and cats, and contains most, if not all, of the active principles in the anterior lobe of the ox hypophysis. An unfractionated pituitary extract, which had no detectable diabetogenic action when tested on the intact normal dog but otherwise resembled crude pituitary extract in general activity, was obtained by allowing the sterile crude extract of fresh ox pituitary gland to remain at room temperature for four months. This preparation will be described as extract ND.1. An extract of acetone-desiccated ox anterior lobe powder, which had been stored in the laboratory in a dry condition for some months, was prepared in a manner essentially similar to that for the extract of fresh tissue. This preparation, which was also non-diabetogenic in normal dogs, but resembled crude pituitary

extract in exhibiting manifold activities, will be referred to as extract ND.2. These three unfractionated extracts were of such concentration that 1 c.cm. contained in each case the material extracted from 250 mg. of fresh anterior lobe tissue or its equivalent—i.e., approximately 50 mg. of dried tissue.

A preparation of prolactin, which was obtained by the Bates-Riddle method and which was highly pancreotropic, was used in one experiment. This was the same preparation as that used previously in investigations on pancreotropic activity in rats (Marks and Young, 1940).

All injections were made subcutaneously with aseptic precautions.

Estimations.—Urinary sugar was determined by Benedict's method and urinary ketones by the method of van Slyke. Nitrogen estimations on food, urine, and faeces were arrived at by the Kjeldahl method. Although frequent analyses for the nitrogen content of food were made, these, and faecal nitrogen determinations, were not carried out daily, so that the figures for nitrogen balance are not quantitatively precise, although on the whole the results were agreeably constant. Blood-sugar determinations were made on capillary blood by the Hagedorn-Jensen method.

Action of Crude Pituitary Extract

(*a*) *Normal Adult Dogs.*—In eight experiments on four dogs (2 male, 2 female) averaging 10 kg. in weight, 5 c.cm. of extract injected subcutaneously each day never failed to produce a substantial glycosuria within seven days. The mean time of the appearance of glycosuria was 5 days (maximum 7, minimum 4) and the average sugar excretion was 23 gm. (maximum 44, minimum 11) on the first day and 58 gm. (maximum 74, minimum 39) on the second day of the diabetic state. The amount of extract required by the subcutaneous route is thus very much less than that necessary when the injections are given intraperitoneally (Young, 1938; Houssay, Foglia, and Smyth, 1941). We have found our adult dogs remarkably constant in their response to this extract, and it seems reasonable to assume that 0.5 c.cm./kg. (equivalent to 25 mg. dry weight of anterior lobe tissue per kilogramme of body weight), administered subcutaneously each day for at least a week, is more than enough to induce a temporary diabetic condition in adult dogs.

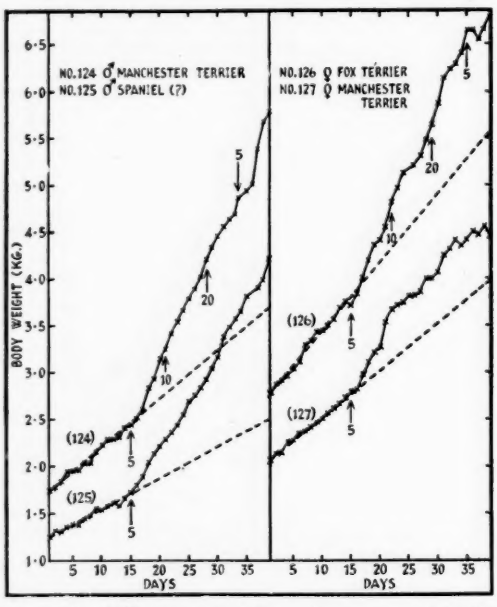

FIG. 1.—The influence of daily subcutaneous injections of crude anterior pituitary extract on the body weights of puppies. The figures below the arrows indicate the daily dose of extract, in c.cm., given from that day onwards. The dotted lines represent the best straight line fitted to the data for the pre-treatment control period.

(*b*) *Normal Puppies.*—Each day four puppies (2 male, 2 female) were given subcutaneous injections of crude extract that were very much larger per kg. of body weight than those required to produce diabetes in adult dogs (Fig. 1). Two of the puppies (Nos. 124 and 126, Fig. 1) received daily doses of extract which progressively increased from 5 to 20 c.cm./day, and then fell to 5 c.cm. again, while the other two (Nos. 125 and 127) received 5 c.cm./day throughout. Three of the puppies showed no trace of urinary sugar at all, while No. 124 gave a trace on the fifth, sixth, and ninth days of treatment, the maximum twenty-four-hour yield being 1.6 gm. (0.5 gm./kg.) on the sixth day of treatment. No trace of ketone was found in the urine at any time. On the basis of these results we can assume that an average dose of 3.3 c.cm./kg. is not an effective diabetogenic agent in the puppy, this being more than six times the dose fully effective in the adult animal. After a total of 19 weeks' treatment No. 124 had reached a weight of 20 kg., compared with the weight of about 8 kg. which he would have attained if his average pre-treatment rate of growth had been continually maintained over this period. At this time he presented the characteristic features of experimental gigantism in dogs, as described in the classical experiments of H. M. Evans—large paws and head, thick and heavy bones, excessive growth of skin, etc. Up to this time he had been sugar-free despite the continuation of daily injections, but later a gradually increasing glycosuria became apparent. At present, after 23 weeks of treatment, his glycosuria has risen to nearly 200 gm. daily and he has stopped growing, his weight having remained around 20.5 kg. for the last three weeks. Nos. 125 and 126, which have received daily injections for 23 and 19 weeks respectively, have not responded to the prolonged growth-promoting action of the extract so strikingly as dog 124, nor have they yet developed a diabetic condition.

Action of Non-diabetogenic Extracts on Pituitary-diabetic Dogs

If the nitrogen-retaining action of pituitary extracts is mediated by the pancreas, as Mirsky (1939) has suggested, then non-diabetogenic pituitary extracts which are pancreotropic (Marks and Young, 1940) might be expected to cause nitrogen retention, increase in weight, and an alleviation of the diabetic condition of at least a temporary duration in animals which are diabetic but have some secretory islet tissue remaining.

In the experiments carried out in this connexion, a single injection of extract was administered to diabetic dogs after a suitable control period. As might be expected, it was found that the response to any given extract was apparently determined by the intensity of the diabetic condition of the treated animal. Thus treatment with a preparation of prolactin which in the rat test is highly pancreotropic (Marks and Young, 1940) permanently increased the D/N quotient of moderately diabetic dog 115 (Fig. 2, A), inducing a sharp rise in ketonuria, which,

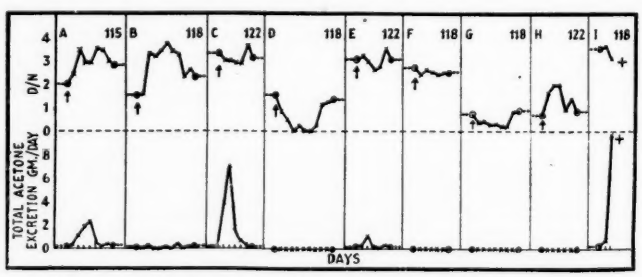

FIG. 2.—Influence of a single subcutaneous injection of various anterior pituitary extracts on the course of diabetes in pituitary-diabetic dogs. The injection was given on the days indicated by the arrows. The initial and final points on each curve represent average values for approximately one week. The intermediate points represent daily values.

Experiment A, Dog 115: Injection of 160 mg. of prolactin
" B, " 118: " " 5 c.cm. of extract ND.1
" C, " 122: " " " " " "
" D, " 118: " " 5 c.cm. of extract ND.2
" E, " 122: " " " " " "
" F, " 118: " " " " " "
" G, " 118: " " " " " " at a time when the dog was receiving 5 units of protamine-zinc-insulin daily
" H, " 122: Injection of 5 c.cm. of extract ND.2 when the dog was receiving 15 units of P.-Z.-I. daily
" I, " 118: Injection of 5 c.cm. of extract ND.2

however, was only temporary. It must be emphasized that this preparation was non-diabetogenic when tested in large doses in the intact adult dog (Young, 1938), and the same is true of all the extracts considered in the present section. The sustained rise in D/N quotient occasioned by a single injection of this extract suggests that permanent damage had occurred to that pancreatic islet tissue which was still capable of secreting insulin.

Extract ND.1, also pancreotropic in the rat, raised the D/N quotient of mildly diabetic dog 118 (Fig. 2, B) from an initial control value of 1.5 to a final approximately constant figure of 2.3 with a substantial loss of nitrogen and of body weight (B in Table). Again permanent islet damage seems to be indicated.

Table showing the Influence of a Single Injection of Anterior Pituitary Extract on the Condition of Diabetic Dog 118

Exp. (Fig. 2)	Length of Period (Days)	Treatment (Single Injection of Extract)	Food Intake (Cals. Daily)	Sugar Excreted (Gm./Day)	Corrected D/N	Nitrogen Balance (Gm./Day)	Change in Body Weight (Gm./Day)
B	4	Control	1,520	63	1·58	−0·5	0
	7	5 c.cm. ND.1	1,420	121	3·10	−4·2	−100
D	7	Control	1,140	52	1·54	−3·5	−35
	8	5 c.cm. ND.2	1,380	15	0·33	+5·0	+50
F	7	Control	1,850	107	2·32	+1·9	+30
	7	5 c.cm. ND.2	1,910	127	2·45	−3·1	−60
G	7	Control (5 U. of P.-Z.-I. daily)	1,200	33	0·78	—	0
	7	5 c.cm. ND.2 (5 U. of P.-Z.-I. daily)	1,200	14	0·39	+4·2	+100
I	10	Control	900	81	3·60	−2·7	−55
	1	5 c.cm. ND.2	900	99	3·64	−2·9	0
	1	—	620	87	3·19	−13·6	−650

(The data given are the average daily values for the various periods.)

When dog 122, whose D/N quotient was at a level of 3.4, was given a single dose of the same extract the only obvious effect was a sharp but unsustained rise in ketonuria. It is interesting to recall that when pituitary-diabetic dogs which are exhibiting a maximal D/N quotient associated with a substantial ketonuria are given a small daily dose of insulin, the D/N quotient may be largely unaffected while the ketonuria may be strikingly reduced (Marks and Young, 1939). The response of dog 122 to a single injection of the pituitary extract (Fig. 2, C)—a response which is similar to that obtained with many other dogs under comparable conditions—seems to be the converse of that with insulin described earlier, and to indicate that the main effect of the extract has been temporarily to neutralize the action of what little insulin the damaged islets are still capable of secreting.

When dog 118 was in a mildly diabetic state he responded to a single injection of extract ND.2 by a temporary but striking fall in the D/N quotient (Fig. 2, D), with a retention of nitrogen and an increase in body weight (D in Table); but later, when his diabetic condition had become more severe, with a control D/N quotient of 2.3, he resembled dog 122 (Fig. 2, E) and failed to show any very obvious response to an injection of the same extract (Fig. 2, F; F in Table). When, however, the diabetic condition of dog 118 was partially controlled by insulin therapy he again showed a temporary fall in D/N quotient in response to a single injection of the same extract (Fig. 2, G), with nitrogen retention and rise in body weight (G in Table), although the opposite result occurred when dog 122 received an injection of the same extract at a time when his diabetic condition had been reduced to about the same degree of intensity by insulin therapy (Fig. 2, H). Finally, when dog 118 had become severely diabetic, with a control D/N quotient of 3.6 and a daily ketonuria of about 0.3 gm. of total acetone, a single injection of extract ND.2, which previously had temporarily alleviated his diabetic condition, now killed him in diabetic coma (Fig. 2, I), with a rapid loss of nitrogen and of body weight (I in Table) and a terminal blood-sugar level of 0.56%.

From the data for the various experiments on dog 118, given in the Table, it is clear that when treatment with extract alleviated the diabetic condition it also induced nitrogen retention and an increase in body weight (D and G in Table), but that if the conditions were such that a single injection of extract exacerbated the diabetes it also induced loss of nitrogen and of body weight (B and I in Table).

Discussion

The present observations indicate that if the extracts used by H. M. Evans in his classical experiments concerning the influence of growth-promoting pituitary preparation on puppies had been fully diabetogenic when tested on adult dogs a condition of diabetes would not be expected to develop in treated puppies until after many months' daily injections, if at all. Thus it is possible to produce experimental gigantism without diabetes, even though the pituitary extracts used are diabetogenic in adult dogs or cats.

The results of this and previous investigations show that the same pituitary extract may be essentially growth (weight)-promoting, or essentially diabetogenic, according to the age of the animal and the adequacy of its pancreatic function. In the intact adult animal (dog or cat) both responses may be manifest simultaneously, although the diabetogenic effect ultimately becomes predominant; while in the young puppy the only obvious response to treatment with the same extract is that of accelerated growth. The fact that with normal cats and normal dogs an increase in body weight is associated with the induction of a diabetic condition by the administration of crude pituitary extract has already been emphasized (Young, 1937, 1938). Now, Ogilvie (1937) has presented quantitative evidence that human infants have a greater amount of pancreatic islet tissue in proportion to body weight than adults. If such a difference holds for the puppy and the adult dog, then the resistance of the puppy to the diabetogenic action of pituitary extracts which are highly effective in the adult dog receives a simple explanation. Furthermore, Langfeldt (1920) found that partially depancreatized puppies, which had been deprived of a sufficient proportion of pancreas to provide a reasonable expectation of the appearance of diabetes in an adult dog, not only were free from all symptoms of diabetes for many months after the operation but in some instances showed an increase of sugar tolerance. Eventually, however, the sugar tolerance declined and a progressive and ultimately fatal diabetes became manifest. The present results concerning the diabetogenic action of anterior pituitary extracts in puppies are in many ways analogous to those of Langfeldt.

The results of our experiments on the influence of pituitary extracts on diabetic adult dogs (Fig. 1 and Table) are consistent with Mirsky's idea that the nitrogen-retaining action of the extract is mediated by the islets of Langerhans, but it should be pointed out that Gaebler and Galbraith (1941), as the result of investigations with completely depancreatized dogs, do not believe that pancreatic insulin is the only factor concerned. Indeed, Gaebler and Robinson (1941) have recently found that on depancreatized bitches receiving a constant dosage of insulin prolactin exerted only a mild diabetogenic action but induced some storage of nitrogen. Clearly some action other than a pancreotropic one was exerted by the pituitary preparation in this instance. The present results are not incompatible with such an action, but under the conditions of our experiments it seems reasonable to assume that the main nitrogen-retaining action of the extracts used was mediated by the pancreatic islets. If this is so, the differences in response to the same extract with differences in intensity of the diabetic condition can be reasonably explained in terms of two antagonistic effects—pancreotropic and diabetes-intensifying (diabetogenic ?)—of the extract, the first tending to induce secretion of insulin with nitrogen retention and an increase in body weight, while the second

intensifies, or tends to intensify, the diabetic condition, presumably by suppression of carbohydrate oxidation, etc. (Russell, 1938), or perhaps by increased sugar formation from fatty acids (Soskin, 1941). If the pancreatic islets are capable of responding to the pancreotropic action of the extract to a sufficient extent when the diabetes is uncontrolled (exp. D, Fig. 2 and Table), or after it has been partially controlled by insulin with consequent rehabilitation of islet tissue and insulin storage (exp. G), then the diabetes-intensifying action of the extract may be completely overcome (however, cf. exp. H), so that treatment with the extract causes temporary alleviation of the diabetic condition, with an increase in body weight and storage of nitrogen. But if the islets cannot respond to the pancreotropic action of the extract to such an extent the extract may have no obvious effect (exp. F, Fig. 2 and Table), or may cause an intensification of the diabetic condition which may be only temporary (exp. C and H) or may lead to death in coma (exp. I). With an extract possessing enough diabetes-intensifying activity, a suitable animal may show a persistent exacerbation of the diabetic condition (exp. A and B, Fig. 2) which is presumably associated with permanent damage to the tissue of the pancreatic islets. Gaebler (Gaebler and Zimmerman, 1939-40) found that pituitary extracts which caused growth and nitrogen retention in normal animals showed a marked diabetogenic action in depancreatized thyroidectomized bitches receiving adequate insulin therapy. Phloridzinized animals reacted, on the other hand, by a rise of body weight and nitrogen retention, with diminished glucose excretion and a constant D/N quotient (Gaebler and Zimmerman, 1939-40). In connexion with the action of our extracts in causing temporary alleviation of the symptoms of pituitary-diabetic animals, with a fall in D/N quotient, it is interesting to note that Haist, Campbell, and Best (1940) find that when such dogs are given a series of injections of crude pituitary extract during a period of fasting, together with very large injections of insulin at frequent intervals, the sugar tolerance of the animals may subsequently show substantial improvement.

It is undesirable to enter here into a discussion of the identities of the active principles concerned, but it should be pointed out that the results indicate that the pancreotropic factor in anterior pituitary extracts is not identical with the diabetes-intensifying factor.* Thus in experiments B and D (Fig. 2 and Table), in both of which dog 118 was initially at the same level of intensity of diabetes, a single injection of one extract induced temporary though marked alleviation of the diabetic condition (exp. D), whereas a different extract raised the D/N quotient and apparently caused permanent damage to islet tissue (exp. B). It therefore seems that the two factors—pancreotropic and diabetes-intensifying—are present in different proportions in these two extracts, and thus cannot be identical. Nevertheless, differential inactivation of different active groupings carried by the same (protein ?) vector cannot be left out of consideration, and the same possibility applies to the previously demonstrated non-identity of the pancreotropic and diabetogenic (intact dog) factors (Marks and Young, 1940). But as we have no evidence on this point it will not be further considered.

Although extracts which are devoid of diabetogenic activity when administered in large doses to the intact dog are capable of intensifying the diabetes of diabetic animals (cf. also Long, 1937), we do not know whether extracts with diabetogenic activity differ quantitatively or qualitatively from those with only diabetes-intensifying action in the diabetic animal, but it should be emphasized that diabetes-intensifying activity can be completely masked if an extract possesses enough pancreotropic activity and the treated animal has enough responsive islet tissue (exp. D, Fig. 2 and Table).

The presence in the human infant of a large proportion of islet tissue (Ogilvie, 1937) is probably associated with the importance of insulin for nitrogen retention, etc., during the period of growth. If an infant were submitted to a long period of low-grade pituitary overaction the pancreatic islets might at first respond with hypertrophy, so that the child would possess capacity for a greater degree of nitrogen retention and growth. The islets might be incapable of sustaining indefinitely such an intensified activity, and once the general blood-sugar level rose irreparable derangement of islet function might result in persistent diabetes. In the adult person the hypertrophic phase of islet response would, analogously, result in an increase in body weight, and it is of particular interest that Ogilvie (1933, 1935) found that a large proportion of the obese subjects he examined revealed hypertrophy of the pancreatic islets. If such a condition is a pre-diabetic one an extra-pancreatic cause of the diabetes seems extremely probable. Is it therefore unreasonable to suppose that the increase in weight of the pre-diabetic human adult may have an origin similar to that seen in the normal adult dog (and cat) treated with anterior pituitary extract—namely, a slight, and possibly ill-sustained, increase in anterior pituitary action? Such a slight increase in pituitary activity as would be necessary to induce a rise of body weight would not necessarily be associated with obvious symptoms of gigantism or acromegaly; nor would it be expected, at least in the majority of cases, to endow the plasma of the patients with anti-insulin activity, demonstrable in tests on rabbits. Even in diabetes associated with frank acromegaly, insulin sensitivity is comparable to that found in normal diabetes (Coggeshall and Root, 1940). Although this question lies outside the scope of the present investigation, it may be suggested that where obvious adiposity of the human pre-diabetic adult exists it may well arise, to some extent at least, from changes in dietary habits (cf. Himsworth and Marshall, 1935; Richter and Schmidt, 1941) possibly resulting from the inhibition of glucose oxidation by pituitary principles (Russell, 1938).

Conclusion

If the above arguments be accepted the pre-diabetic increase of height in children and of weight in the adult can be regarded as a reactive or protective mechanism for the storage of the carbohydrate of which the oxidation is suppressed, and of the nitrogen which is retained, under the influence of anterior pituitary action. The expansive capacity of the adult is definitely limited, and unless the child is capable of sustained excessive growth (the limit to which may be the capacity of the islets to hypertrophy) there will come a point, as was probably the case with dog 124, at which the carbohydrate the oxidation of which is inhibited can no longer be completely stored in the form of extra body tissue. Sugar then leaks into the blood stream, and despite a subsequent and complete subsidence of pituitary overactivity, permanent stigmata may remain in the form of islet lesions and a persistently diabetic condition. It is interesting to note that the rat, which is capable of substantial and sustained response to the growth-promoting action of pituitary extract even in ripe old age, is almost completely resistant to the diabetogenic action of crude pituitary extract (Young, 1938), although sensitivity can be induced by partial pancreatectomy (Long,

* The word "diabetauxetic" (Greek αὔξειν, to increase), analogous with "diabetogenic," might be useful to describe factors which are capable of intensifying the diabetic condition where diabetes already exists but which are not obviously diabetogenic in suitable intact animals. Similarly, "diabetostatic" might be used to describe factors capable of alleviating the intensity of a diabetic condition by inducing the pancreas to secrete more insulin.

1937, 1939). The above interpretation of experimental findings cannot in any sense be considered as attempting to exclude the possibility that clinical diabetes may result, in some instances, from primary changes in the pancreatic islets—e.g., those which follow interference with the pancreatic blood supply, and in haemochromatosis (cf. Warren, 1938). Nevertheless, the large number of cases of diabetes in which a definite increase in the mass of the body is apparently a proleptic feature may reasonably be supposed to result from a pancreatic - pituitary imbalance occurring at a level of pancreatic islet activity higher than that operative in the normal animal.

Summary

When puppies are treated daily with doses of crude pituitary extract greatly in excess of those required to produce diabetes in adult dogs they respond with an increased growth rate but do not exhibit symptoms of diabetes. When one puppy was treated daily for nearly five months it eventually became intensely diabetic, and then stopped growing despite continuation of treatment.

When adult dogs that have been rendered permanently diabetic by a short period of pituitary treatment are given a single injection of pancreotropic pituitary extracts, which produces no detectable diabetogenic activity in normal adult dogs, the response may be a transitory attenuation of the diabetic condition with nitrogen retention and increase of body weight, or an exacerbation of the diabetes with loss of nitrogen and of body weight; intermediate responses were also obtained. These differences in response are believed to result largely from differences in functional capacity of pancreatic islet tissue.

It is suggested that an increase in body weight, associated with an increase in function of the pancreatic islets, can be regarded as neutralizing, for a time at least, the diabetogenic influence of the anterior pituitary gland. It is therefore possible that the excessive weight of the adult diabetic patient and the abnormal height of the diabetic child (White) indicate an increased pituitary function which may be of temporary duration only, and of which the diabetogenic action may be completely masked for a time by a protective increase in pancreatic islet activity, induced by the pancreotropic action of the gland. Such a condition might lead first to an increase in the mass of the body and eventually to diabetes.

The preparation of the extract used in this investigation was largely carried out by my assistant E. A. Woollett, and the sterilizing filtration by F. A. Holbrook. For the skill and perseverance of these two technical assistants I wish to express my thanks and gratitude.

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TREATMENT OF PULMONARY TUBERCULOSIS BY THORACOPLASTY

BY

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Pulmonary tuberculosis is a disease whose incidence rapidly increases during wartime, and it is important in the present situation that the treatment of this condition should remain in the forefront of discussion. From the public health point of view no patient who is suffering from pulmonary tuberculosis should return to work until his sputum is negative. In our crowded factories and offices any such person with a sputum positive for tubercle bacilli is an anachronism, and subversive both to the health of the community and to the war effort. Under the present conditions of long hours of work, continued stress, and minimal nutrition the dissemination of the disease from one such focus may be considerable.

Thoracoplasty is applicable as a line of treatment to only a small percentage of cases of pulmonary tuberculosis. The results are, however, satisfactory in that in most cases the patient, previously a public menace, becomes non-infective and is able to return to some form of useful occupation.

The following is an account of the indications for thoracoplasty in the treatment of pulmonary tuberculosis as used by the team working at the surgical clinic of the Lancashire County Council Tuberculosis Service at High Carley Sanatorium, Ulverston.

Indications for advising Thoracoplasty

This is probably one of the most difficult problems in the whole of surgery. Only by the closest team-work between the surgeons, the staff of the sanatorium, and the anaesthetist can these cases be accurately assessed. The cases are divided into two groups—those regarded as "good risks" and those as "justifiable risks." The latter group will contain a number of patients suffering from advanced disease in which the risks of thoracoplasty are greatly above the average. These risks are, however, permissible because there is a definite possibility that by running them the disease may be arrested, and because by no other method of treatment can the patient's life be saved. Apart from the consideration of the individual patient, there is another cogent reason why the immediate and ultimate chances of the patient must be most fully weighed. Sanatorium life is such an intimate one that every patient is fully aware of the results of operative treatment on others, and in order that those in the "good" class shall have no misgivings as to the outcome of their operation the fullest confidence in the results of thoracoplasty must be maintained.

There are certain general principles which influence the selection of cases:

1. The tuberculous lesion must be undergoing fibrosis and must not be in a state of acute exudation. Rapid compression of the lung, such as occurs by thoracoplasty, is likely, in cases with an acute exudative lesion, to cause a rapid dissemination of the disease with infiltration of the same or opposite side. If, however, the disease is in a reparative stage—i.e., under-

going fibrosis—the lung will stand this rapid compression without such risk of further spread of the tuberculous lesion. A lung lesion which is healing by fibrosis without coexisting cavity formation can become bacillus-free, can heal, and can probably remain healed without the need for operative intervention, though the end-result may be benefited by hemidiaphragmatic paralysis. It is the persistence of chronic cavitation that constitutes the danger to the patient and to the community. A chronic fibrotic case without clinical or radiological evidence of cavitation which does not become bacillus-free should be tomographed, when the presence of cavities will almost certainly be demonstrable. The large majority of cases coming up for consideration for thoracoplasty are those in which a cavity or cavities have failed to close as a result of sanatorium treatment and in which an artificial pneumothorax has proved impossible or ineffectual. Most of these cases have very definite symptoms: the sputum is abundant and loaded with tubercle bacilli, and they may be persistently pyrexial. The general health of others, as a result of prolonged sanatorium treatment, may be good ; in some, even, the cavity may be dry, the sputum (if any) tubercle-free, and the symptoms minimal. It may seem drastic to recommend a major operation such as thoracoplasty to patients who are apparently well enough to return to their homes and even to work. The long view must be taken, however, from both the individual and the public health aspects. Sooner or later the disease will light up again, as a result either of overwork or of a coryza or influenza. Not only may the disease spread to those parts of the lung or lungs previously involved, but, more serious still, the patient will become an infecting agent for a shorter or longer time before again being taken under control.

Repeated haemoptyses, whether or not associated with obvious cavitation, provide an additional indication for thoracoplasty, as does also a chronic non-productive irritable cough following upon distortion of the trachea and bronchi due to massive pulmonary fibrosis consequent on partially healed tuberculosis.

2. The main tuberculous lesion must be unilateral. After a total thoracoplasty the patient has only the lung on the opposite side left with which to breathe. If there is an active tuberculous lesion, however small, in this remaining lung, there is considerable likelihood that this lesion will increase and will eventually prove fatal. An old lesion on the contralateral side which is radiologically and clinically healed should still be viewed with suspicion, as any extra work of that lung may cause it to reactivate. It must be remembered that the tubercle bacilli, although surrounded by dense fibrous tissue, are in most cases merely dormant and not dead. Calcification may be taken as a fair indication of death of the tubercle bacilli. The final assessment of the condition of the opposite lung must be based on the clinical examination, and never solely on the radiographic appearances. The slightest evidence of activity should cause the decision for operation to be postponed, pending a further period of rest in bed. Crepitations which are persistently present and unaltered at the opposite apex are not a contraindication. These cases with contralateral evidence of disease or instability are included in the "justifiable risk" group. It is in the assessment of such doubtful cases that the opinion of the medical superintendent of the sanatorium is of great value to the team. A pronounced opinion by him, as a result of his continuous observation of any individual patient, will often tip the scale when decision is in the balance.

3. The size and position of the cavities will influence the decision as to whether thoracoplasty will be of permanent benefit. It may be asserted as a general rule that the smaller the cavity and the less extensive the lesion the easier it is to obtain complete control by a thoracoplasty. Complete control of cavities near the hilum or in the base is more difficult than control of those in the upper lobe. Large cavities, especially if surrounded by a thick wall of fibrous tissue, are not readily compressed. Extensiveness of the disease, provided it is unilateral, is no contraindication.

4. As pneumothorax is the simplest form of collapse therapy it should have been tried in all cases. If the pneumothorax is impossible, or is producing inefficient collapse of the affected area which cannot be improved satisfactorily by internal pneumolysis, then thoracoplasty must be considered. Any residual pneumothorax should be allowed to reabsorb or be removed before thoracoplasty is attempted, as collapse of the ribs is prevented when there is a cushion of air between these and the lung.

5. Although no absolute age limits can be given it is generally inadvisable to perform a thoracoplasty for pulmonary tuberculosis under 15 years or over 45 years of age. In children it is inadvisable owing to the exudative form of disease that occurs and also the subsequent effect on growth. In the more elderly the cardiovascular changes and the diminished ability of the remaining lung to compensate for the loss of aerating surface may be contraindications. Exceptions to this rule are, however, not uncommon.

6. The better the general condition of the patient the greater is the probability of success. Once it is accepted in a given case that healing of the lesion cannot be obtained except by a thoracoplasty, then, however well stabilized the patient may be for the time being, it is wrong to wait for the period of decline to set in. When, on the other hand, the general condition is poor the operation must be deferred in the hope that improvement can be effected by bed rest, even at the risk of a relapse or extension of the disease during this period of delay. Amyloid disease if advanced will contraindicate operation, but if mild this should clear up when the pulmonary lesion heals following thoracoplasty. A transient gastro-enteritis will delay operation, but an established tuberculous enteritis is a direct contraindication. Involvement of the larynx does not necessarily prohibit operation unless there is ulceration causing pain or oedema producing stridor: healing will be promoted once the infection in the lungs has been obliterated. The presence of other lesions, such as bone and joint tuberculosis and genito-urinary tuberculosis, only contraindicates operation if these are advanced. Anaemia should be treated by haematinics. The main thing to be remembered is that tuberculosis is a general disease of which the lung lesion is but a local manifestation. The lung is, however, in most cases the important lesion, and as such should be given prior consideration. Elimination of the pulmonary focus will cause improvement elsewhere. If the patient is the subject of recurrent bronchitic attacks or has an asthmatic tendency, thoracoplasty should not be undertaken.

The Operation

The standard operation employed at this clinic is the ten-rib paravertebral thoracoplasty with removal of the transverse processes, done occasionally in two, but more often in three, stages. Partial thoracoplasties are rarely undertaken. This procedure is considered only in the type of case with extremely limited disease in one apex, and then as an alternative to an extrapleural pneumothorax. Most lungs with apical lesions show involvement to some degree, generally of the mid-zone, and often of the lower zone. Furthermore, the lymphatic interconnexions between the various parts of the lung are so numerous that the tuberculous infection extends over a much wider area than the clinical or radiological evidence would suggest. The partial collapse of a lung produces between the collapsed and uncollapsed portions of the lung a line of tissue strain in which it is no infrequent occurrence to see later a reactivation of the disease. It is admitted that in some cases a total thoracoplasty does produce an apparently unnecessary collapse of seemingly healthy lung with some resultant loss of vital capacity, but it is felt that the disease is much more securely arrested.

Anaesthesia is produced by a preliminary induction with 6 to 10 c.cm. of intravenous barbiturate, followed by inhalation of oxygen with 3 to 5% of chloroform vapour to maintain narcosis. Infiltration of the whole operative area is undertaken with 1% kerocain (procaine), and at the stage of rib exposure the intercostal nerves are infiltrated as they pass out on to the neck of the ribs. It is our opinion that, while the operation is performed essentially under local anaesthesia, light narcosis should be maintained throughout.

The first stage of the operation consists in the removal of the whole of the first and second ribs up to the costal cartilages and 13 cm. of the posterior ends of the third and fourth ribs. The third and fourth transverse processes are also removed. At the second stage, undertaken fourteen days later, 13 cm. of the fifth to eighth ribs inclusive are removed together with the transverse processes. At the final stage, a fortnight after, 13 cm. of the ninth and tenth ribs are removed. Occasionally the operation is performed in two stages by removing five ribs at each stage. The wound is drained for twenty-four hours through a separate stab incision.

Considerable pressure is maintained laterally and anteriorly on the collapsed portion of the chest after the first twenty-four hours by means of elastic strapping and pads of wool and sorbo rubber. Weights are applied later on to the front of the chest to assist the collapse, and finally an elastic brace is fitted which maintains constant pressure on the chest for some months. Exercises are given to counteract the tendency to scoliosis and to regain full arm movements. Rest in bed is continued for two to three months after the operation.

Results

During the period 1933-40 59 cases of pulmonary tuberculosis were treated by thoracoplasty; 52 were for parenchymatous disease and 7 for tuberculous empyema. 158 operations in all have been performed on these patients. The follow-up results, undertaken in May, 1941, are as follows:

TABLE I.—*Cases of Parenchymatous Disease*

	Fit and Well, with Negative Sputum	Unfit or with Positive Sputum	Now Dead	Total
1933 ..	1 (100%)	—	—	1
1935 ..	3 (100%)	—	—	3
1936 ..	5 (62·5%)	1	2	8
1937 ..	4 (67%)	—	2	6
1938 ..	8 (67%)	2	2	12
1939 ..	4 (57%)	2	1	7
1940 ..	10 (67%)	4	1	15
Total ..	35 (68%)	9 (17%)	8 (15%)	52

35 patients (68%) are now fit and well, and 30 (88%) of these are able to do their daily work. Nine are still unfit or have a positive sputum (see Table V). Eight patients have died since the operation was undertaken. No death due to post-operative shock occurred, but four of these patients died within three months of the operation. Details of the cases can be seen by reference to Table V (Cases 8, 11, 14, 15, 20, 21, 34, 48).

Of the 52 patients 40 were considered "good risk" cases for thoracoplasty and 12 "justifiable risks" (see Fig.). The results in these two groups were as follows:

TABLE II

	Good Risk	Justifiable Risk
Fit and well, with negative sputum ..	30 (75%)	5 (41·7%)
Unfit or with positive sputum	5 (12·5%)	4 (33·3%)
Now dead	5 (12·5%)	3 (25%)
Total	40	12

There is a tendency to increase the number of "justifiable risks" operated upon, and in some of the later cases the disease would have been deemed extensive enough to contraindicate operation in the early days. A further analysis of the "justifiable risk" group of cases reveals the following figures:

TABLE III

	Fit	Unfit	Dead	Total
1935	1	—	—	1
1936	—	1	1	2
1938	—	2	1	3
1939	—	—	1	1
1940	4	1	—	5

It is as yet too early to forecast the outcome in the 1940 group of "justifiable risk" cases, but one feels a certain degree of apprehension regarding their future. It is possible that by performing total thoracoplasty in this group too much strain is put on the remaining lung, and that a more localized thoracoplasty with maintenance of function of the lower part of the lung may produce better results. It is still important, however, in assessing the line of treatment in this group, to bear in mind the objections to localized thoracoplasty which have been mentioned before.

It is interesting to study the group of cases with large cavities—i.e., 5 cm. or more as measured on the A.-P. radiograph.

TABLE IV

Size of Cavity	Fit	Unfit	Dead
5 cm.	4	—	—
6 cm.	1	3	—
7 cm.	2	1	—
8 cm.	—	1	—
9 cm.	—	—	1

The value of thoracoplasty in producing collapse of giant cavities has been disputed, and it would appear from this small group of cases that patients with cavities of certainly 6 cm., or over, would be better treated by preliminary suction drainage to reduce the size.

The only satisfactory criterion by which to assess the results of thoracoplasty is a comparison with a similar group of cases in which thoracoplasty has not been done —i.e., those refusing operation. Unfortunately it has not been possible to obtain any figure for such cases from this centre, but they would at any rate be very few in number. Comparable figures have, however, been published by Hurford (1941) and Freedlander and Wolpaw (1937) which show that in the operated group the disease was arrested in 65% (Hurford) and 57% (Freedlander and Wolpaw), and in the unoperated group in 16% (Hurford) and 10% (Freedlander and Wolpaw).

Approximately 50% of all cases considered for possible thoracoplasty on presentation of the history and films are turned down on clinical examination owing to the presence of too active disease on the opposite side or to the general condition of the patient not being up to standard. The cardiovascular system of many of these patients is in an unstable condition due to continued toxaemia, and would be an added hazard to the operation. As more and more experience is gained in this branch of surgery there is a tendency to perform thoracoplasty on increasingly "desperate" cases, with the idea of giving the patient a chance to recover. While such a procedure is justifiable, as death is certain in so many cases in one to two years, the danger of bringing the operation into disrepute must always, as mentioned before, encourage a certain degree of conservatism.

How soon should thoracoplasty be undertaken in these cases of fibro-cavernous disease? There is probably a growing tendency to operate earlier, but any degree of exudation must delay thoracoplasty until fibrosis has occurred. Moreover, the exposure of a patient to the risks and consequences of a major operation before every

other method of treatment has been given the fullest trial is deprecated. It is possible that the advent of surgery has encouraged a tendency to haste in the treatment of a disease in which time, bed rest, and sanatorium treatment are essential principles.

One feature of this operation is the scoliosis that occurs towards the side on which the thoracoplasty has been undertaken. The degree of scoliosis is probably somewhat greater if the transverse processes have been removed than if they have been left, owing to the temporary loss of attachment of the erector spinae group of muscles. This, however, can very effectively be overcome by encouraging the patient to lie on the operated side from the beginning. The degree of scoliosis appears more severe in the radiograph than on clinical examination. When the patient is clothed the deformity is negligible. The advantage claimed for the more efficient collapse of the lung when the transverse processes are removed in our opinion outweighs the

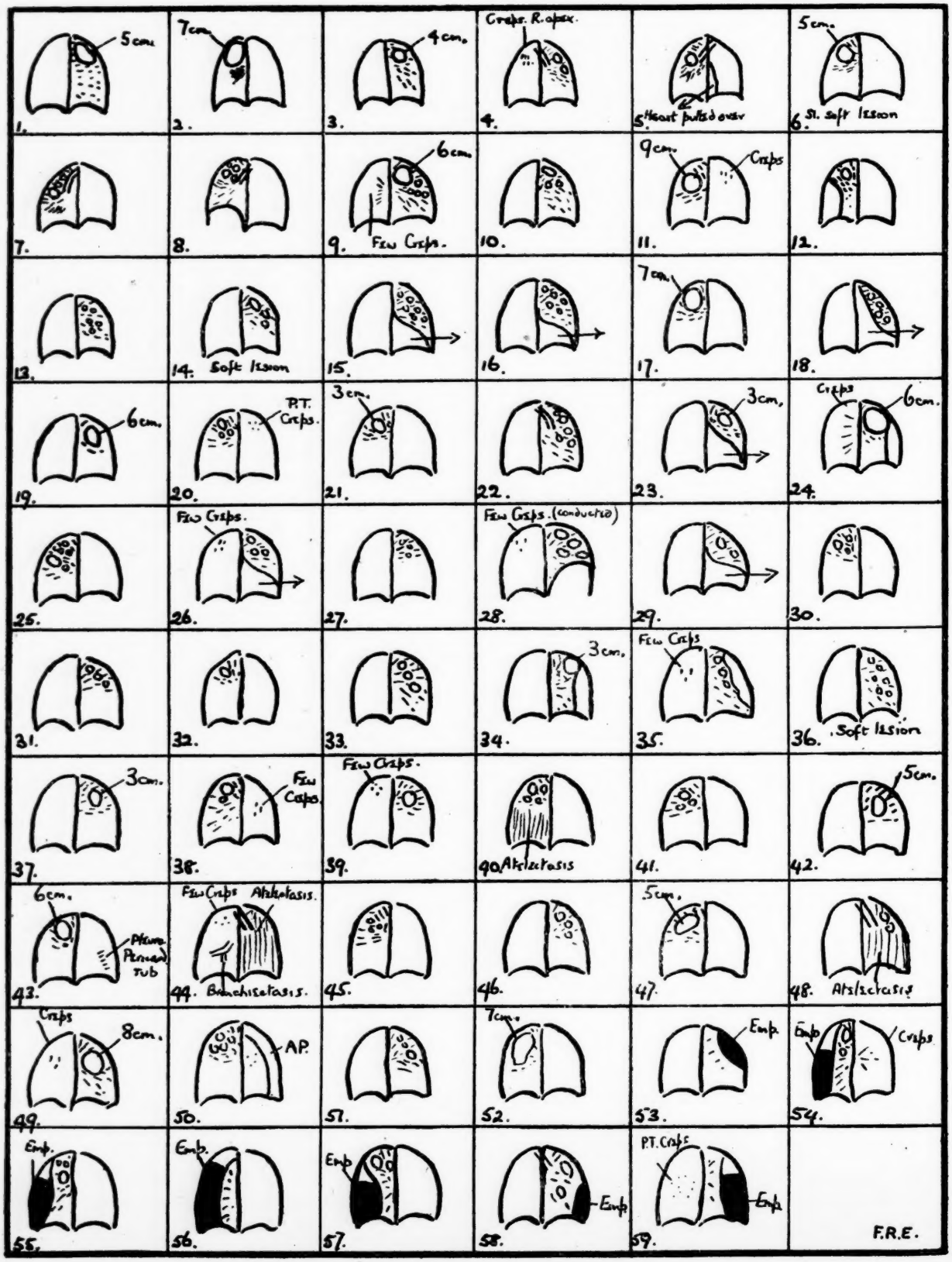

TABLE V

Case	Sex	Age	Length of Disease in Years	Previous Collapse Therapy	Risk Classification	Pre-thoracoplasty: Sputum T.B.	Pre-thoracoplasty: Sputum Amount in oz.	Post-thoracoplasty: When Sputum became Negative for T.B.	Post-thoracoplasty: When Patient discharged from Sanatorium	Condition in May, 1941: Sputum T.B.	Condition in May, 1941: Sputum Amount in oz.	Condition in May, 1941: Scoliosis	Condition in May, 1941: General Condition	Condition in May, 1941: Working	Remarks
Parenchymatous Disease															
1933															
1	F	28	3	p.	G	+	¼	2 years	2½ years	–	tr.	o	Fit	Yes	
1935															
2	F	22	3	ap. ip.	G	+	2	Immed.	7 months	–	nil	++	,,	,,	
3	F	26	7	p.	G	–	0	—	7 months	–	,,	o	,,	,,	
4	F	26	5	—	JR	+	tr.	6 months	11 months	–	,,	o	,,	,,	8 ribs only
1936															
5	M	20	3	ap.	G	+	tr.	Immed.	6 months	–	,,	+	,,	,,	
6	F	26	1	—	G	+	2	,,	7 months	–	,,	+	,,	,,	
7	M	19	2	—	G	+	1½	,,	8 months	–	,,	+	,,	Unemp.	
8	F	20	2	ap.	G	+	½	3 months	6 months	Died 2 years later. Spread opposite side					
9	F	25	4	—	JR	+	3	6 months	8 months	+	1	+	Unfit	No	
10	F	24	1	ap.	G	+	2½	Immed.	1 year	–	nil	+	Fit	Yes	
11	F	31	4	—	JR	+	3	—	ND	Died 9 months later. Spread opposite side					
12	F	36	5	—	G	+	1½	Immed.	7 months	–	nil	+	Fit	Yes	
1937															
13	F	36	3	—	G	+	2	1 month	7 months	–	,,	+	,,	,,	
14	F	25	2	ap.	G	+	5	—	ND	Died 18 months later. Spread opposite side					
15	F	14	7	—	G	+	3	—	ND	Died 3 months later. Toxaemia					
16	M	20	1	ap.	G	+	1	Immed.	6 months	–	nil	+	Fit	Yes	
17	F	38	5	ap. ip.	G	+	2	1 month	6 months	–	,,	+	,,	,,	Cavity not completely closed
18	F	29	6	—	G	+	1	Immed.	6 months	–	tr.	+	,,	,,	
1938															
19	F	28	1	pc.	G	+	½	2 months	5 months	–	nil	++	,,	,,	
20	F	22	5	pc.	JR	+	1	—	ND	Died 10 days after 1st stage. Acute Tb. bronchopneumonia					
21	F	39	1	—	G	+	⅛	—	ND	Died 18 months later. Lobar pneumonia. Probably non-tuberculous					
22	M	36	15	—	G	+	½	Immed.	5 months	–	nil	o	Fit	Yes	
23	M	26	6	ap. pc.	G	+	1	1 month	1 year	–	tr.	o	,,	,,	
24	M	31	3	ap. pc.	JR	+	3½	—	1 year	+	2	+	Unfit	No	Cavitating opp. side
25	F	25	3	—	G	+	¼	Immed.	1 year	–	tr.	++	Fit	Yes	
26	F	36	8	ap.	JR	+	⅛	,,	2 years	+	½	+	Unfit	No	Cavitating opp. side 4 months after op.
27	M	35	4	—	G	+	tr.	,,	10 months	–	nil	+	Fit	Yes	
28	F	32	7	p.	G	+	3	3 months	10 months	–	,,	+	,,	No	Rather dyspnoeic
29	F	26	4	—	G	+	1	6 weeks	5 months	–	,,	+	,,	Yes	
30	F	41	1	—	G	+	½	6 months	8 months	–	tr.	+	,,	,,	
1939															
31	F	32	2	—	G	+	½	Immed.	4 months	–	nil	++	,,	,,	
32	M	27	6	—	G	+	2½	1 month	8 months	–	,,	+	,,	,,	
33	M	38	9	—	G	+	3	14 months	4 months	–	1	+	Unfit	No	Multiple Tb. lesions
34	F	28	6	ap.	G	+	1	—	ND	Died 17 days after 1st stage. Tb. bronchopneumonia. Diarrhoea. ? origin					
35	F	26	3	ap. ip. pc.	JR	+	¼	2 months	6 months	+	⅛	+	Unfit	No	Readmit. 2 mths. later with sprd. opp. side
36	M	38	4	pc.	G	+	1	Immed.	6 months	–	tr.	+	,,	,,	Tiredness; cavity still just visible
37	F	23	3	ap. pc.	G	–	¼	—	10 months	–	tr.	+	Fit	Yes	
1940															
38	F	21	3	ap.	JR	+	tr.	3 months	4 months	–	tr.	+	,,	,,	
39	M	40	4	ap. ip. pc.	JR	+	½	9 months	ND	+	tr.	+	Unfit	No	Cavity still present
40	F	26	7	—	G	+	¼	Immed.	4 months	–	nil	+	Fit	Yes	
41	F	22	1	—	G	+	⅛	2 months	11 months	–	,,	+	,,	,,	
42	F	29	3	—	G	+	2	1 month	11 months	–	,,	+	,,	,,	
43	M	33	2	ap.	JR	+	2	2 months	ND	+	1	+	Unfit	No	Cavitation opp. side
44	F	27	7	—	JR	+	2	Immed.	6 months	–	1	+	Fit	Yes	Associated bronchiectasis
45	M	30	8	—	G	+	tr.	,,	4 months	–	nil	+	,,	,,	
46	M	34	3	—	G	+	2	—	ND	+	½	+	Unfit	No	Cavity still present
47	M	37	3	—	G	+	2	Immed.	6 months	–	tr.	+	Fit	,,	
48	F	39	17	—	G	+	⅛	,,	ND	Died 3 months later with acute spread to opposite side					
49	M	34	12	ap.	JR	+	1½	6 weeks	ND	–	tr.	o	Unfit	No	
50	M	28	7	p.	G	+	½	9 months	11 months	–	tr.	++	Fit	Yes	
51	F	33	7	pc.	G	+	½	Immed.	6 months	–	tr.	++	,,	,,	
52	M	24	2	ap.	G	+	1	1 month	ND	Positive sputum recurred 3 months later. Cavity not obliterated. For further collapse					
Tuberculous Empyemata															
1937															
53	F	31	3	—	JR	+	20 BF	—	ND	Died 3 weeks after 1st stage. Toxaemia					
54	F	24	2	ap.	JR	+	1	—	ND	Died 2 years later from spread to opposite side					
55	M	26	8	ap.	JR	+	11 BF	—	ND	Died 2 months later from spread to opposite side					
1938															
56	M	26	4	ap.	JR	+	1	2 months	ND	–	nil	+	Unfit	No	Still needs small plastic op.
57	M	24	3	ap.	JR	+	1½	—	15 months	+	tr.	+	,,	,,	Losing weight
1939															
58	M	29	9	ap.	JR	+	2	—	ND	Died 9 months later from toxaemia and G.U. tuberculosis					
1940															
59	F	26	2	—	JR	+	12 BF	—	ND	Died 14 days after 1st stage. Toxaemia and amyloid disease					

Previous Collapse Therapy : ap., Artificial pneumothorax. ip., Internal pneumolysis. pc., Phrenic crush. p., Phrenicectomy.
Risk Classification : G, Good risk. JR, Justifiable risk.
Scoliosis : o, No scoliosis. +, Slight scoliosis. ++, Moderate or severe scoliosis.
Sputum : tr., Trace. BF, Bronchial fistula.
Discharge : ND, Not discharged.

resulting scoliosis. All too often, when the transverse processes are left, the persistence of an elongated, flattened, but not wholly obliterated cavity can be seen in the costo-vertebral sulcus.

Tuberculous Empyema.—Of the seven subjects of tuberculous empyema treated by thoracoplasty, five are dead, one is alive but deteriorating, and one is well and cured of his tuberculous empyema but still requires a small plastic operation to complete the epithelization of the remains of the cavity. All cases had been treated conservatively for a long period before being presented for thoracoplasty. Operation undertaken at an earlier date before the general effects of the continued toxaemia become too marked and the pleural membranes too thickened would undoubtedly produce more satisfactory results.

Summary

From the public health point of view no person with a sputum positive for tubercle bacilli should be at large in the community.

Thoracoplasty will arrest the disease in a certain proportion of cases and allow return to work.

Indications for thoracoplasty are: The disease should be in the fibrotic stage, and must be mainly unilateral; pneumothorax should have been tried; the cavities should not be too large. The age limit is given as 15 to 45, with exceptions. The general condition of the patient should be good.

Ten-rib paravertebral thoracoplasty with removal of the transverse processes is the operation of choice.

Results at the surgical clinic of the Lancashire County Council Tuberculosis Service in the period 1933-40, with follow-up in May, 1941, are given. Fifty-two cases were operated on for parenchymatous disease: 35 (67%) are fit and well, with negative sputum, and 30 (86%) of these are working.

Seven cases were operated on for tuberculous empyema, with total arrest of the disease in one case only. These cases should be operated on earlier.

Our thanks are due to Dr. G. Lissant Cox, Central Tuberculosis Officer, Lancashire County Council, for permission to publish this report. We acknowledge the great help given to us by the tuberculosis officers of the county in the follow-up of these cases. Our greatest appreciation is due to the members of the medical and nursing staff of High Carley Sanatorium for the after-care of these most difficult patients. The anaesthesia was conducted by Dr. John Halton.

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To meet urgent needs, some of them arising out of the war, four new teaching departments have been set up at Leeds General Infirmary. One is a department of thoracic surgery, another is a school of physiotherapy, the third is a school of radiography and radiotherapy, and the fourth is a school of dietetics. An account of these developments is given in the *Yorkshire Post* of November 21. The thoracic surgery department is especially noteworthy, and by its inauguration Leeds becomes the first of the teaching hospitals in the Provinces to take this step. The founding of the school of physiotherapy has been expedited by the war, for the establishment of such a school, with its own building, was until lately no more than a suggestion for post-war development. Damage to London hospitals has led to the immediate demand for a physiotherapeutic instructional centre elsewhere. The course at Leeds will occupy two and a half years, and is intended to prepare students for the examination of the Chartered Society of Massage and Medical Gymnastics. At the school of radiography and radiotherapy students are in training for the examination of the Society of Radiographers during a two-year course which, as a war measure, will be reduced to six months. The school of dietetics gives six months' practical training for those who have done the theoretical work at a college of domestic science. It will function in close contact with the special kitchen set apart by the Leeds General Infirmary for the preparation of food for patients on a special diet.

AN IMPROVED METHOD OF REGIONAL ANAESTHESIA IN ACUTE ABDOMINAL SURGERY

BY

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The advantages of regional anaesthesia in *grave abdominal cases* have long been recognized. While in America and on the Continent the work of such pioneers as Crile, Labat, Finsterer, and others has been received with enthusiasm, regional anaesthesia has never achieved popularity in this country. This, we think, is because (1) most patients dislike being conscious during an operation; (2) the administration of a regional anaesthetic is often in itself an ordeal for even the most stoical patient; (3) too often anaesthesia proves to be incomplete, and deep general narcosis is found necessary.

Types of Regional Anaesthesia

The forms of regional anaesthesia in use to-day are as follows:

Spinal Anaesthesia.—(*a*) Subarachnoid Block:—By this method an extreme degree of relaxation of the abdominal muscles is obtained together with what Farr describes as "negative intra-abdominal pressure." If the anaesthetic ascends as high as D 5 splanchnic block is also obtained. The liability to grave falls in blood pressure and the risks of sudden collapse make spinal anaesthesia (subarachnoid block) unsafe except in comparatively fit patients. (*b*) Epidural Block:—The work of Dogliotti (1933) and Odom (1936) aroused interest in this method. It is now generally considered that epidural block is neither reliable nor safe.

Field Block.—This method is the most popular in use owing to its comparative safety and ease of administration, and may well be associated with the work of Finsterer (1923). Although anaesthesia at the site of incision is usually adequate, relaxation is often poor; this is a serious defect in an exploratory operation. "Negative intra-abdominal pressure" is absent, and protrusion of the abdominal viscera often occurs, especially if the patient strains; this may be aggravated by inadequate preliminary sedation and rough handling of the viscera by the surgeon. Sometimes, after the abdomen has been opened, it becomes clear that the first incision must be extended or a fresh incision made; local infiltration or additional field block may then be necessary if deep general narcosis is to be avoided. To protect the patient from the effects of traction on the viscera, field block is often supplemented by splanchnic block, the most popular technique being that of Braun (1924).

Infiltration Anaesthesia.—This method, so strongly advocated by Farr (1930), has recently been used by Vishnevsky (1938), Synovich (1940), and Novikov (1940). Injection of large quantities of dilute anaesthetic solution—e.g., equal parts of 0.25% novocain and 1 in 4,000 percaine—into the fascial pockets surrounding muscles and viscera generally requires the use of a power-driven pump; the aspiration test cannot be performed, and there is always risk of mechanical breakdown. Infiltration anaesthesia carries with it all the disadvantages of field block.

Bilateral Paravertebral Block.—If a true paravertebral block is performed in the manner originally suggested by Sellheim (1905) and perfected by Labat (1922) then the rami

communicantes and the sympathetic nerves are blocked as well as the intercostal nerves. If this procedure is repeated bilaterally from D 7 to D 12 then excellent abdominal anaesthesia and relaxation occur; a substitute for splanchnic block is, in addition, obtained. Unfortunately this otherwise excellent method has grave disadvantages. Skill above the average is required to place the point of the needle at the exit of the vertical foramen. The difficulty of accurate injection makes this method unreliable. Ever present is the well-known danger of injecting anaesthetic solution into the prolongations of the subarachnoid space along the spinal-nerve roots. The all-important aspiration test may then be wrongly interpreted owing to cerebrospinal fluid being colourless. Paravertebral block is not a practical proposition in the hands of the average anaesthetist and surgeon.

Bilateral Mid-axillary Intercostal Block.—Here the intercostal nerves are injected in the mid-axillary line, generally from D 7 to D 11. This method has always enjoyed a certain amount of popularity, and quite recently has been recommended by Bartlett (1940). It has the disadvantage that having injected the intercostal nerves on one side the anaesthetist must change position, prepare the skin, and repeat the injections on the other. If the anaesthetist wishes to perform splanchnic block by the posterior approach of Kappis, which for reasons stated later we prefer to the anterior approach of Braun, the patient must undergo a change of posture, with fresh skin preparation and rearrangement of towels.

An Improved Method of Regional Anaesthesia

We believe that the method here recorded is free from the major disadvantages of the techniques described above. It has six main features: (1) adequate pre-operative omnopon (pantopon) sedation; (2) the preliminary use of a short-acting barbiturate—e.g., hexobarbitone *B.P.* (evipan); (3) posterior bilateral thoracic-nerve block; (4) bilateral splanchnic block by the posterior approach; (5) oxygen therapy with the B.L.B. mask; and (6) attention to gentleness in operative technique. A detailed description of the method follows.

Preliminary Sedation

If no sedative has been given before admission, or if sedation has been inadequate, then as soon as consent for operation has been obtained the patient receives an intravenous injection of omnopon. We use the drug intravenously because of its rapid action by this route and because, by giving it slowly, the dose can be regulated to the patient's requirements. The respiratory rate should not be depressed below 14 to the minute. A small dose of atropine (1/100 grain) is given subcutaneously half an hour before operation.

Surgical Preparation

In the ward a radiant-heat cradle is used, the foot of the bed is raised, and when required, as in cases of intestinal obstruction, the stomach is emptied by a small-calibre tube (Ryle or Miller Abbott), which is left in position both during and after operation. Intravenous infusion is employed when necessary: in cases of profuse vomiting, intravenous glucose saline is given; plasma or blood is used as indicated. A B.L.B. mask is applied when anoxia is suspected and in cases of intestinal obstruction with distension (Fine, Hermanson, and Frehling, 1938). When the condition of the patient has improved the abdomen and back are prepared in the usual way.

Preliminary Intravenous Narcosis

If the patient's condition permits, intravenous hexobarbitone *B.P.* (evipan) is given in the anaesthetic room. Should further omnopon sedation appear necessary we find that drawing up 1/3 grain of omnopon into the evipan solution is a safe and useful procedure provided the resulting straw-coloured solution is introduced with extra slowness and caution. One of us (N. R. J.) has used this method since 1937. We prefer evipan to pentothal because after a "single" dose it gives a long light narcosis without undue depression of the respiratory and cardiovascular centres. Evipan does not diminish the oxygen capacity of the blood (Pask, 1941). Intravenous evipan with omnopon sedation not only renders the patient unconscious during the insertion of the regional anaesthetic but, if a suitable dose has been given, keeps him asleep throughout even a long abdominal operation if no unanaesthetized area is stimulated. The benefits of light general narcosis supplementing regional anaesthesia and thus preventing psychic trauma were first emphasized by Crile and Lower (1920), and were recently referred to by Hewer (1940). The short-acting intravenous barbiturates—e.g., evipan—are particularly useful in that they protect against the toxic effects of regional anaesthetic solutions (Rovenstine and Cullen, 1939). Moreover, they are portable, easy to administer, and non-inflammable—virtues which are especially important in war surgery. Should the patient's condition be so grave as to make him apathetic to his surroundings, then supplementary intravenous narcosis is used only if he becomes restless during operation. It is omitted in cases of severe vomiting, for then the risk of inhaling vomitus is present even though continuous gastric aspiration is employed. The importance of maintaining a clear airway cannot be emphasized too strongly. We use a naso-pharyngeal tube, made by cutting an old Magill's endotracheal tube of suitable diameter to a length equal to the distance between the lobe of the patient's ear and the alae nasae. A safety-pin is inserted through the non-bevelled end to prevent the tube being inhaled. If this short tube is placed correctly it is tolerated even in very light narcosis.

Regional Anaesthesia

Preparation of Solution.—Wearing sterile gloves, the anaesthetist prepares a 1% solution of novocain with adrenaline. We take two 1-gramme sterile ampoules of planocaine and dissolve the contents in 200 c.cm. of sterile normal saline to which is added, from a sterile ampoule, 0.5 c.cm. of 1 in 1,000 adrenaline. The sterile 10-c.cm. syringe (we use the Lundy type) and needles, which have been previously sterilized by boiling and allowed to cool gradually, are washed through with cold sterile water.

Technique of Posterior Bilateral Thoracic-nerve Block.—The patient is turned on to his left side and the vertebral column is flexed by an assistant as in spinal anaesthesia, care being taken that the airway is maintained. A small pillow is, when necessary, placed under the loin to prevent sagging of the lumbar spine. The skin is painted with 1 in 1,000 flavine in spirit and the highest points in the iliac crests are palpated to determine the intercristal line. Immediately below this line lies the fourth lumbar space, and from here the first lumbar space and then the tip of the first lumbar spine are identified. A point is taken 6 to 8 cm. (3 or 4 fingerbreadths) lateral to this spine, and here a 10-cm. needle is inserted to rest on the twelfth rib at its lower border. The syringe is now attached, and the point of the needle is made to slip off the lower border of the rib and is advanced for a distance of not more than 1 cm. The needle point now lies in the region of the neurovascular bundle, but it is difficult to know when it is just in the right fascial plane. It is therefore important that, as the injection is given, a to-and-fro movement of the needle is made; only in this way can one be sure of "hitting off" the nerve. A total of 8 c.cm. of the anaesthetic solution

is injected, and this subcostal injection is repeated up to and including D 6. The whole process is then repeated on the other side. In thin patients the ribs can be palpated, but in obese or muscular subjects they must be found by exploration with the needle. This is not difficult, but it should be noted that the tenth and eleventh intercostal spaces are appreciably wider than the preceding ones. Anaesthesia by this method is easy to perform and is associated with good relaxation of the abdominal muscles and with "negative intra-abdominal pressure." This last factor is very important in acute abdominal surgery.

Technique of Splanchnic Block.—We use a 0.5% solution of novocain with adrenaline; this we obtain by adding an equal quantity of saline to the 1% solution remaining from the thoracic-nerve block. At the site of injection of the twelfth dorsal nerve a 12-cm. needle is introduced at an angle of 45 degrees to the median plane and is advanced until its point strikes the body of the first lumbar vertebra. The needle is then partly withdrawn and advanced again more tangentially, and the procedure is repeated until the needle is felt to slide past the body of the vertebra for a distance of not more than 1 cm. If no flow of blood occurs 1 c.cm. of 0.5% anaesthetic solution is injected to clear the needle. The aspiration test is performed carefully and, if negative, the remaining 9 c.cm. is injected; the aspiration test is repeated at least once during this injection. A total of 30 to 40 c.cm. is given in this way, and the technique is repeated on the other side. It is important that the needle point should lie in the loose retroperitoneal areolar tissue and not within the substance of the crus of the diaphragm. Some indication of its true position is given by the feel of the piston as the injection is made; if the needle is placed correctly the piston is pressed home without resistance. We prefer to use this posterior approach of Kappis (1914) because: (1) the block is inserted and has time to take effect before the operation has begun; (2) the intra-abdominal manipulations of the anterior approach are avoided; (3) the anterior approach cannot be performed efficiently except through an upper abdominal incision; and (4) we have found it an efficient and safe method. Hewer states that "experimental injections made in the post-mortem room with methylene blue showed that this technique does soak the splanchnic area efficiently." He also states that "posterior splanchnic block is a reasonably safe procedure if carried out with all precautions."

Management of the Patient on the Table.—The patient is lifted on to the operating table and a pillow is placed under the knees. This small degree of hip-joint flexion improves relaxation of the abdominal wall. The legs are held in position by a padded strap passed over the thighs just above the knees. The patient's head rests on one pillow, and the hands are placed under the head in the "sun-bathing" position. The arms in this position may easily be controlled and a further intravenous injection may readily be given, if required.

Oxygen Therapy

We believe that in all grave cases oxygen therapy is of great utility. We have used it as a routine, and have come to regard it of value in every case not only during operation but also pre- and post-operatively. Waters, Wineland, and Seevers (1931) have pointed out that morphine and the barbiturates are two of the many factors which may cause anoxia in the surgical patient. We use a B.L.B. mask with all ports closed, the oxygen flow being adjusted to 6 to 8 litres a minute. A flowmeter should always be employed, as the flow of oxygen may be inadequate though the bag may appear to be filling properly. A reducing valve should be used if available.

Points in Operative Technique

(*a*) The towel clips should not include the skin. (*b*) An adequate incision is important: a little extra length often allows the operation to be carried out with ease and without undue traction on the viscera. (*c*) A vaselined glove makes insertion of the hand and exploration of the abdomen a much less traumatic procedure. (*d*) The adoption of the Trendelenburg position in the lower abdomen and of the reversed Trendelenburg in the upper abdomen allows the intestines to fall away and often obviates the use of intraperitoneal packs. (*e*) A gentle operative technique is essential throughout. Retractors and packing should be avoided where possible, and traction on all tissues should be gentle and gradual.

Scope and Indications

We are aware that we are describing no new technique of regional anaesthesia, but we believe we have evolved a method by which its long-recognized advantages in acute abdominal surgery can be put to practical use. Regional anaesthesia is often supplemented by "light" inhalation narcosis, but in many of such cases we have observed that the inhalation narcosis has been anything but light and the regional anaesthesia in reality superfluous. While the method we describe is useful in "interval" surgery, we believe it to be of most value in the "poor risk" acute abdomen. We consider that, where possible, the patient should not undergo the ordeal of being conscious during the administration of a regional anaesthetic or during the subsequent operation. *The advent of the short-acting barbiturates has in our opinion revolutionized the possibilities of regional anaesthesia.* We have found that after adequate preliminary omnopon a single intravenous injection of evipan (usually 0.5 to 1 gramme in the "poor risk" abdomen) keeps the patient asleep throughout even a long abdominal operation if no unanaesthetized area is stimulated. In experienced hands the method we describe is safe and reliable and is not difficult to perform. It does require practice, and the anaesthetist must be fully conversant with the use and dangers of intravenous narcosis. The application of this method to abdominal war surgery should be of value.

Summary

The various types of regional anaesthesia in present use are discussed. A new method is described. It combines: (1) adequate pre-operative omnopon sedation; (2) the preliminary use of hexobarbitone *B.P.* (evipan) in preference to pentothal: (3) posterior bilateral thoracic-nerve block from D 6 to D 12 inclusive; (4) bilateral splanchnic block by the posterior approach of Kappis; and (5) pre-operative, operative, and post-operative oxygen therapy, using the B.L.B. mask.

The importance of gentle operative technique is stressed.

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TRICHINIASIS IN BIRMINGHAM

BY

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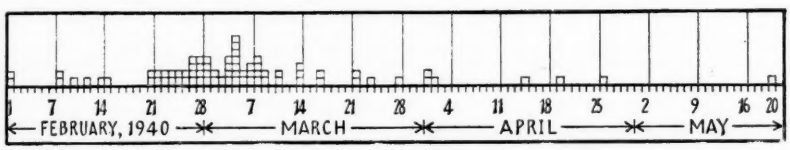
An outbreak of trichiniasis occurred in Birmingham during the months of February, March, and April, 1941. Seventy-eight definite cases were reported. The first was notified to the Public Health Department with a doubtful diagnosis of trichiniasis on February 24. By this time it was known that the disease was abroad. Accounts had been published of cases in Wolverhampton (Sheldon, 1941; Lee, 1941) and in Hertfordshire (Garrod and Maclean, 1941). A warning against eating undercooked pork or sausage had been broadcast by wireless, and similar warnings had appeared in the Birmingham press.

The course of the epidemic is illustrated in the graph: it will be observed that isolated cases occurred before and after the main outbreak. Female patients predominated (81%). Six children were affected, the youngest a girl aged 4.



Dates of onset of symptoms of 75 cases of trichiniasis occurring in Birmingham administrative area. Vertical divisions are weeks and days. One small square = 1 case. Two additional cases had onsets on January 10 and June 15 respectively. In one other case the date of onset was uncertain. Doubtful cases omitted.

Clinical Findings

In general the clinical features corresponded closely with those described by Sheldon and by Lee.

Oedema.—The most constant feature (occurring in all cases but one) was oedema of the eyelids: this was to be expected, since it was made the main criterion of preliminary diagnosis. It was of a constant and characteristic type. It was nearly always symmetrical; in only one definite case in this series and in one doubtful case was it unilateral. The whole eye-socket filled up, and in the severest cases vision was totally occluded for a few hours. It tended to spread down to the angles of the jaws. The patients were often totally unrecognizable, and appeared bloated, coarse, and much older than their years. The oedema was in most cases the initial symptom, preceding by only a few hours the other characteristic features of the "toxic" stage of the disease—fever, malaise, and generalized pains. It persisted for about a week in the moderately severe cases, and occasionally for considerably longer. Its subsidence was gradual as a rule, and there was a tendency to recurrence, especially at night-time. Oedema elsewhere than in the face and eyelids may well have occurred unnoticed in many cases, for in those in which it was observed it was slight and was mainly at the wrists and ankles. Nevertheless the most remarkable feature of the oedema is its localization.

Frontal or orbital *headache* was common at the onset, and was occasionally the most distressing symptom. *Conjunctival injection*, slight or severe, was the rule; in three instances there were subconjunctival haemorrhages, which in one case took the form of rings round the corneo-scleral junctions. I saw no subungual haemorrhages, though I sought them regularly. *Fever*, as evidenced by temperature records, delirium, sweating, or flushes, was observed in 30 cases. It probably occurred in many more. Where repeated observations were made it was high and remitting (e.g., 100° to 104°) for the first few days, usually returning almost to normal during the second week. The tendency was, of course, for these observations to be made upon the severer cases. *Malaise*—i.e., a general sense of ill-being—was constant in the first few days in all but the mildest cases. It was present even in the absence of other evidence of pyrexia. *Muscular pains* or stiffness occurred in 60 patients, either with the oedema or, more often, a few hours afterwards. The site was variable. A characteristic onset was of pain between the shoulder-blades, spreading up the back of the neck to the occipital region. Later the limbs were usually affected, and in the severer cases pain and stiffness were generalized. The pain was severe, aching or cramping in quality; it was worse on movement, especially after rest. There was often stiffness, weakness, or numbness of the limbs.

Gastro-intestinal symptoms—anorexia, nausea, vomiting, abdominal pain, constipation, or diarrhoea—occurred in 39 patients. In 9 these symptoms clearly and definitely preceded the "toxic" stage, and were pronounced: and it may justifiably be surmised that they represented that point in the disease when the worms are establishing themselves in the mucous membrane of the bowel. It is interesting to note that of these 9 patients no fewer than 6 (67%) gave a history of having consumed raw sausage, whereas of the remaining 69 cases only 7 (10%) admitted to this. I attribute this significant difference to the larger dosage of viable larvae in the raw sausage. A *rash* was present in 8 only of the definite cases. In 7 of these it was urticarial in type, and coincided with the oedema. This type of rash might perhaps have been expected more often in view of the other points of similarity (oedema and eosinophilia) to allergic conditions. Indeed, urticarial rashes were the commonest cause of difficulty in diagnosis (see below). Evidences of affection of the *nervous system* were few in this outbreak. A varying degree of drowsiness, lethargy, or listlessness was frequently present, and in three patients this amounted to stupor. One patient developed a transient quadriplegia. Two patients complained of pronounced dimness of vision for a few hours at the height of the illness.

The *severity* of the disease was difficult to assess, since I saw most of the patients on a single occasion only, and at various stages of their illness. Many of the patients were acutely ill, but I think it is true to say that in no case did the condition give rise to grave anxiety—the pulse and respirations remained good throughout. There were no deaths.

Diagnosis

The main criteria of diagnosis were oedema of the eyelids and eosinophilia. For practical purposes it was found necessary to decide upon an arbitrary scheme of diagnosis, and the following standards were adopted:

1. Diagnosis definite—trichiniasis:		
(*a*) Eosinophilia 10% or more	70	78
(*b*) ,, 5-9%; definite clinical picture	6	
(*c*) No eosinophil count; definite clinical picture	2	
2. Diagnosis doubtful:		
(*a*) Eosinophilia 5-9%; doubtful clinical picture	3	8
(*b*) ,, less than 5%; suggestive clinical picture	3	
(*c*) Investigation incomplete; suggestive clinical picture	2	
3. Not trichiniasis:		
Eosinophilia less than 5% (or not measured); unconvincing clinical picture		16
Total		102

The eosinophilia is discussed more fully below. A "definite clinical picture" required oedema of the eyelids of pronounced degree and characteristic type without other apparent cause, or a lesser degree of oedema together with

muscular pains. It is realized that there are possibilities of error in this scheme, since other causes of oedema and of eosinophilia exist, and a mild or atypical trichiniasis may not present these features.

Group 3 were all cases notified as ? trichiniasis. They included urticarial and other rashes (9), frequently with some degree of oedema of the face or lids; "influenza" or "rheumatism"—i.e., muscular pains with or without fever or catarrh (2); mild degrees of facial oedema without other characteristic symptoms (2); paratyphoid fever (1); slight malaise without any characteristic symptoms (1); and undiagnosed pyrexia with facial oedema (1).

Biopsy was performed on two patients. In one case trichinella larvae were present in the excised muscle; in the other no larvae were found, but the muscle (gastrocnemius) showed degeneration of the fibres and infiltration by eosinophil cells. The latter patient had a 65% eosinophilia on the fortieth day of disease.

Many of the earlier cases were diagnosed only in retrospect—i.e., after it had become known that trichiniasis was about. They had for the most part been labelled "influenza," "gastric influenza," "kidney trouble," or "rheumatism." There is reason to suppose that many cases never came to the notice of the Health Department at all, either through failure in diagnosis or because they were too mild for treatment to be sought.

Blood Cell Changes

The presence and degree of *eosinophilia*, as stated above, was taken as one of the main criteria in diagnosis. Differential white cell counts were made on all but two of the cases and at various stages of the disease; it was not practicable to perform total counts, except in a few cases treated in hospital. The degree of eosinophilia showed little correlation with the day of disease. For instance, two cases of comparable severity had 5% and 44% respectively on the thirty-first day of illness. The greatest degrees of eosinophilia recorded in this series were 61% on the fourteenth day and 65% on the fortieth. The average was 24%. The reaction developed very early: a patient taken ill with swelling of the eyes and face and abdominal pain had 16% of eosinophils on the day of onset; there had been no previous symptoms. On the other hand, one patient still showed a 10% eosinophilia on the seventy-fifth day after the onset of illness, and another 4% on the 132nd day.

So far as can be judged in the absence of total counts a *lymphocytosis* occurred as well as eosinophilia. This is deduced from the fact that the ratio of neutrophil leucocytes to lymphocytes (large and small together) was markedly and consistently low (average 1.4 as against a normal of about 2.3), and that this ratio tended to fall still lower after the eighth week, when the eosinophilia was disappearing. Had the altered ratio been due to a replacement of neutrophils by eosinophils a return to normal would have been expected as the eosinophilia decreased.

The Intradermal Test

After the subsidence of the outbreak I was able, through the courtesy of Dr. Beeson of the Ministry of Health, to obtain a small quantity of trichinella antigen (a saline extract of desiccated larvae) wherewith to perform the Bachman intradermal test for trichiniasis. This test is stated to become positive about sixteen or seventeen days after infection (van Someren, 1939; Spink and Augustine, 1935), and to remain so for an indefinite period. The reliability of the test has been variously assessed. Calus (1938) found it to be positive in 74% of 66 patients (and in 5% of controls), and Heathman (1936), investigating 57 patients, regarded it as less reliable than the eosinophil count. I was informed, however, that the antigen supplied to me had been found very reliable in recent outbreaks in England, and I hoped it would prove of value in testing the validity of my arbitrary standards of diagnosis. Unfortunately the results were inconsistent in some preliminary tests on known (Group 1*a*) cases. Of 7 of these, 3 were positive, 2 negative, and 2 doubtful. I tested one patient whom I had classified as Group 3 ("not trichiniasis"): he had vomited on two occasions, but had had no other symptoms, and was investigated only because his wife was a doubtful case of trichiniasis. He gave a positive result; his wife was negative.

The results of these few tests are set out in the accompanying table. The numbers are too small for any conclusions to be drawn, except that the test is not by itself a reliable criterion of diagnosis. The reading of the test was complicated by the large proportion (50%) of patients who gave some degree of reaction to the saline solution used as a control. The practical value of the test, except in hospital patients, is also limited by the necessity to remain with the patient for at least half an hour before a positive result can be excluded.

Table showing Results of Bachman Intradermal Test on Eleven Patients

Group	Result of Test			Total
	Positive	Negative	Doubtful	
1*a*	3	2	2	7
2*a*	–	–	1	1
2*b*	–	2	–	2
3	1	–	–	1

Inquiries into Causation

The habit of eating raw sausage reported by Sheldon (1941) and Jolly (1941) as common among people in the Midlands was found to be followed in Birmingham, where 22% of patients admitted to the habit in the past or present. Inquiries covered all forms of pork, but, though 9 patients denied having eaten sausages during a period of two weeks preceding the onset of the illness, in only one case was it felt that a probable source of infection other than sausage had been found. This was a pig's cheek. As one would expect, bacon was found to be the other commonly consumed form of pig-meat; it was not, however, eaten with anything like the frequency of sausage. In view of the inadequate curing of bacon under wartime conditions it has been suggested (Jolly, 1941) that it may convey trichiniasis. In the present investigation this was regarded as improbable in view of the fact that even lightly cooked bacon, being in thin slices, would be expected to reach temperatures lethal to trichinellae. Of the patients who had eaten sausage, only 13 admitted to having eaten it raw; while 19 were emphatic that it had been well cooked. The question of course arises, What degree of cooking is lethal to the trichinella? Also, What temperature is reached in the middle of a fried or grilled sausage? Jolly, quoting American workers, gives the answer to the former question as "55° C., gradually obtained." The latter remains, so far as I know, unanswered.

One is inclined to wonder whether the wartime sausage, with its low meat content and probably high water content, requires more cooking than the pre-war one in order to achieve this temperature throughout. Or perhaps the present-day sausage actually receives less cooking than its predecessor on account of the low fat content, which causes it to brown on the outside more rapidly, or on account of a tendency for inferior casings to burst more easily. These are matters of surmise: what is definite is that many

patients who developed trichiniasis denied with emphasis that they could in any circumstances have eaten raw sausage. A possibly significant point in this connexion is the frequency, almost amounting to regularity, with which the affected person had *cooked* the sausage, whereas usually other members of the family who had also partaken remained unaffected.

Incubation Period

Inquiries as to the number of days elapsing between the consumption of pork and the onset of symptoms yielded little reliable information owing to the difficulty of determining the day of consumption. Among 22 patients in whose case fairly definite information was obtained the average interval was seven days, but the scatter was very wide. One observation which may throw some light on the incubation period is that a group of six cases, isolated in space and time, all started their symptoms on a Saturday. Since chance is a most unlikely explanation of this, I take it to imply that in this group there was a tendency to eat sausages on one particular day of the week, and that there was a fixed incubation period. Three of these patients could give no definite date as to when they had had sausages; the other three had had them regularly on Saturdays. This suggests a seven-day or fourteen-day incubation period for this group, and the evidence pointed rather towards seven days.

Administrative Action

A circular letter was sent to all practitioners and hospitals in Birmingham drawing their attention to the prevalence of the condition, reminding them of the leading symptoms, and requesting them to notify all cases to the medical officer of health. There was some doubt as to whether the condition was compulsorily notifiable. All notified cases were visited by a sanitary inspector and subsequently (except for a few in whose case full information as to clinical picture and blood count was already available) by me. A special form, which included particulars of all pork consumed in the preceding two weeks, was completed. The retailer was visited and inquiries made as to the manufacturer or market. Acting on information thus obtained the chief veterinary officer endeavoured to trace the meat back to the farm or collecting centre. It was soon found that a large number of manufacturers of sausage were involved, including some of the biggest in the city. To trace the sources of the pork used by these manufacturers was far from easy: at that time the farmers were reducing their stock drastically owing to the rationing of feeding-stuffs, and the pigs were gathered together in collecting centres throughout the countryside, and thence distributed, not locally but over wide areas. So that the meat in a sausage eaten by one of our patients might have been derived from any one or more of several districts as far apart as Cornwall and Norfolk. Nor could observations made over a period of time be correlated, since the tendency was for each farm to kill off its whole stock and not to enter the market again.

The result of this inquiry was that fourteen widely separated districts were listed, each of which was connected (often indefinitely) with two, or in one case three, patients. It was felt that the information was not definite enough to justify further investigation at the collecting centres; and no connexion could be established between these districts and those supplying pork to other areas where trichiniasis had appeared.

Consideration was given to the feasibility of microscopically examining specimens of muscle from all sows and boars entering the Birmingham markets, but as the work involved would have been colossal, and this type of inspection had given negative results elsewhere, it was regarded as impracticable. So reliance was placed on warning the people of Birmingham against the dangerous practice of eating raw or imperfectly cooked sausage or pork. This was done by means of notices in the daily press. It is thought that this action, while exerting little effect in terminating the outbreak, was probably influential in reducing the number of persons affected.

Discussion

It cannot be claimed that either the factors producing the outbreak or those terminating it have been at all clearly elucidated. It seems extremely likely that, as suggested by Jolly, the condition has been endemic in the Midlands for a long time, going unrecognized except during an occasional epidemic. If this be so, then it must be assumed that small quantities of trichinous pork are constantly entering the market for human consumption, and also that Midlanders regularly eat raw or undercooked pork. The latter assumption is not difficult to accept: the habit of eating raw sausage is not just a wartime one. The former suggestion is at first sight a reflection on our system of meat inspection, but in practice trichinous pork cannot be detected by ordinary inspection methods, except occasionally in a very well fed animal in which there are pronounced fat deposits at the poles of the cysts, or in very gross and very old infestations when there are many calcified cysts. Regular examination by microscopy is not practised in this country—an omission justified by the rarity of the disease.

Why did the disease suddenly assume epidemic proportions? Attempts to answer this question may follow two lines. It may be supposed that there was a sudden increase in the quantity of trichinous pork thrown on to the market; or it may be argued that changes in their feeding habits made the population suddenly more susceptible to infestation from the pre-existing source. It has already been mentioned that throughout the winter months of 1940-1 farmers were killing off their breeding stock owing to shortage of feeding-stuffs. This meant that many old sows and boars were suddenly turned into sausages. Obviously the older a pig the greater the chance that it will have become trichinosed; furthermore, it is said that these older animals are far more prone than younger ones to kill and eat rats—an additional source of possible infestation which, it has been suggested, may act as a reservoir for trichiniasis in this country. A further reason why swine should become trichinosed during wartime is an alteration in the constitution or diminished care in the cooking of pig-swill. It might have been expected that the cooking of swill would have been carried out with more than ordinary care during recent months in view of the prevalence of foot-and-mouth disease: I am informed, however, that shortage of time and labour has resulted in an increased laxity in this respect. Reasons for believing that people are more likely to become infested with trichiniasis during wartime, irrespective of any increase in the degree of infestation of the pork, have already been adduced. They are (1) the increased consumption of sausage owing to the shortage of other forms of meat; (2) possibly an increase in the local habit of eating sausage-meat raw, associated with an increase in the number of women who go out to work, taking their lunch of sausage-spread with them; (3) alterations in the constitution of the wartime sausage (less meat and fat, more water, and poorer-quality skin) which make for inadequate cooking.

No one of the above factors would account for the appearance and localization of the epidemic: between them they may be held to do so.

Why did the outbreak end? The killing off of old pigs is clearly a self-limited process. The consumption of raw or lightly cooked pork may have been discouraged by propaganda, though I find it hard to believe that its effect would be felt for long. The former is more likely to have been the determining factor.

To sum up, I suggest that the killing off of old stock threw a few trichinosed swine on to the market. These produced overt disease in a few localities, which were determined by the pork-eating habits of the people: there were probably a number of such localities, but in only a few did the disease become prevalent enough to attract attention and thus be diagnosed. The need to slaughter these swine was determined by economic conditions, and was of limited duration.

The outbreaks draw attention to one fact of importance—trichiniasis exists among English swine. It is probably widespread, since the Harpenden cases were believed to be associated with pigs from East Anglia, the Penrith cases with local stock, and the Wolverhampton cases with West Midland stock, while those in Birmingham may have come from any one or more of a number of districts throughout England. The infestation is probably most of the time slight, as regards both the number of pigs affected and the severity of the disease.

I am indebted to Dr. H. P. Newsholme, medical officer of health for Birmingham, for permission to publish this account. It is also a pleasure to record the willingness with which medical practitioners furnished me with particulars of their patients, both in and out of hospital.

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Medical Memoranda

Crush Fracture of Sesamoid Bone of Thumb

That injury to a sesamoid bone may be the cause of the severe pain and disability of a "sprained" or "staved" thumb is suggested by the case reported below. In Pye's *Surgical Handicraft* (eighth edition, 1919, p. 205) there is a picture of an *x*-ray film illustrating a fractured sesamoid of the thumb. The text states: "The skiagram shows the result of a sprain of the thumb sustained by a medical student during a football match, and it will be noticed that the sesamoid bone is fractured; the thumb was forcibly hyperextended, with this result. As far as we know, this is the only case of fractured sesamoid recorded."

A man aged 62 was lightly holding the steering-wheel of his car in his right hand, the thumb being uppermost and pointing forwards and to the left, when he collided with a stationary car which had no tail light. The force of impact, though not great, was transferred through the steering column and wheel to the base of the thumb. He experienced sudden severe pain at the site, followed by stiffness and some swelling. When examined half an hour later the ball of the thumb was generally tender. Active movements of the thumb were impossible, and any attempt at passive movement resulted in great pain. The thumb was held in a semi-flexed position. A radiograph revealed no fracture or dislocation, but the sesamoid bone on the ulnar side showed a crushed appearance: the area of the shadow was increased, while the density was decreased (Figs. 1 and 2). Control films of the other hand confirmed the abnormality (Figs. 3 and 4). The hand was bandaged round a ball of cotton-wool, and complete recovery resulted in a few days.

The frequency with which such injuries occur, without a Bennett fracture or other recognized bony or articular derangement, is so well known that the term "staved" thumb is a household expression. It describes a condition causing a degree of pain and incapacity quite out of proportion to the violence of the injury. Unlike the ordinary sprain of other joints the symptoms pass off completely in a very short time. Bruising may occur, but is by no means common. Slight swelling in the region of the metacarpo-phalangeal joint is present in the early stages. Tenderness over the palmar aspect

FIG. 1.—Injured thumb; back view.

FIG. 2.—Injured thumb; front view.

FIG. 3.—Normal thumb; back view.

FIG. 4.—Normal thumb; front view.

of the joint, extending proximally into the muscles of the thenar eminence, is the most constant sign.

On account of the delicate structure of the sesamoids and the difficulty of demonstrating them clearly on the *x*-ray film, injury to these bones is apt to be overlooked. Effusion into the tendon surrounding the sesamoid exerts pressure on the nerve endings and causes a reflex rigidity of the muscle. It is probable that such an injury exists in most cases in which the symptoms are out of proportion to the signs and appearances.

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Tywardreath, S. Cornwall.

E. Shaffer (*Ohio med. J.*, 1941, **37**, 862) states that 1,575 cases of trichiniasis were reported in the United States during the period 1842-1914, and 2,968 were reported from 1915 to 1936, making a total of 4,543 cases during ninety-four years. The mortality rate for trichiniasis has fallen from 15.4% for 1842-1914 to 4.4% for 1926-36, indicating that more mild cases are now diagnosed and reported than formerly. There is a definite seasonal fluctuation in the occurrence of the disease, with a peak in the winter, particularly after Christmas and New Year holidays. Swine fed on garbage have trichinellae five times as frequently as do grain-fed swine, and are the principal source of human trichiniasis. If municipalities persist in feeding swine with garbage, Shaffer recommends that a law should be made requiring cooking of garbage before it is given to the swine.

Reviews

SULPHONAMIDE CHEMOTHERAPY

Sulfanilamide and Related Compounds in General Practice. By Wesley W. Spink, Associate Professor of Medicine, University of Minnesota Medical School. (Pp. 256. Approximately 16s. 6d.) Chicago: The Year Book Publishers; London: H. K. Lewis and Co., Ltd.

Orthodox lines which have been adopted in several transatlantic books on bacterial chemotherapy are followed in Wesley W. Spink's book. Introductory chapters on general principles and the properties of different compounds are followed by instructions for the treatment of different kinds of infection. Each book on this subject has an ephemeral advantage over its predecessors, and the new features in this are up-to-date descriptions of sulphanilylguanidine and sulphadiazine, as well as a chapter on local application, a subject also referred to in those dealing with dentistry and dermatology.

The greater part of the book is a sound and simple statement of well-established facts, but a much more interesting and debatable feature is the table in which the author has committed himself to a statement of the relative merits of the three principal compounds for treating fifty-seven different conditions. Sulphanilamide is given as the first choice for all haemolytic streptococcal infections, sulphapyridine for all pneumococcal infections except meningitis and septicaemia (for which sulphathiazole is recommended), and sulphathiazole for all staphylococcal infections except meningitis (for which sulphapyridine is recommended). Sulphathiazole is advised for gonorrhoea, sulphapyridine for ophthalmia neonatorum, and sulphanilamide for gonococcal arthritis; different drugs are also recommended for meningococcal infection according to whether the meninges or the blood stream is involved, regardless of the fact that commonly both are. It is only fair to say that this table contains a good many question marks, and the author is to be complimented on so enterprising an attempt, but it would be hard to support some of his decisions by any solid evidence. Two succeeding tables list diseases in which sulphonamide compounds are of doubtful and of no value respectively; anthrax should be expunged from the second of these. A large amount of dogmatic statement is also compressed into a small space in a table of toxic manifestations caused by the same three drugs, twenty-five separate conditions being listed with seven degrees of frequency. "Common" (ranking next to "frequent") is the adjective used of the occurrence of drug fever, dermatitis, hepatic damage, jaundice, and moderate anaemia during treatment with sulphanilamide, and of the first four it is said, "may be serious: discontinue drug." This lurid picture scarcely tallies with common experience. Although these items are open to criticism, the reader will be grateful to the author for expressing his views so plainly and exactly.

STERNAL PUNCTURE

Sternal Puncture: A Method of Clinical and Cytological Investigation. By A. Piney, M.D., M.R.C.P. With a foreword by Lord Horder, M.D., F.R.C.P. (Pp. 77. 12s. 6d. net.) London: Heinemann Medical Books. 1941.

Examination of the bone marrow during life has become progressively easier, as biopsy of the tibia has been followed in succession by sternal trephine and sternal puncture. It is true that needle puncture cannot tell us all that trephining and histological sections can, but its greater simplicity for patient and operator makes it the method of choice in most instances. Increased interest in the bone marrow has been reflected in a growing literature, and shortly before the war articles and monographs on this subject were appearing at an average rate of more than one a week. Most of these were technical and addressed to readers with a working knowledge of haematology, and there is probably still a public for the type of small primer which Dr. A. Piney has just published. After a brief historical introduction the author describes the cytology of the marrow and the "myelogram" or differential count of the normal marrow smear. There follows a description of the myelogram in the various blood disorders, infections, and protozoal diseases.

The book is written with the easy charm which has made Dr. Piney's previous books deservedly popular and should serve a useful purpose in introducing the beginner to this instructive technique. The price seems to us unduly high for a book with only 77 pages and a single small colour plate. Piney follows other authors in stating that the bone marrow in idiopathic hypochromic anaemia is characterized by a predominance of immature normoblasts, most of which are large and strikingly basophilic. Bodley Scott's work suggests that this is not in fact true, the characteristic cell in all iron-deficient marrows being a small, misshapen, polychromatic normoblast with a pyknotic nucleus. The best way to learn the technique of sternal puncture is to watch someone else carrying out the operation. Piney suggests going through the angle of Louis, which is perhaps not the easiest approach, and he does not emphasize that only a small quantity of marrow, 0.1 to 0.2 c.cm., should be aspirated.

A VARIED MEDICAL CAREER

It Passed too Quickly. An Autobiography. By Air Vice-Marshal Sir David Munro, K.C.B., C.I.E., M.B., F.R.C.S.Ed., LL.D. (Pp. 304. 15s. net.) London: George Routledge and Sons, Ltd.

Sir David Munro has led the eventful and happy life that justifies the title of his book. After graduating M.A. at St. Andrews he went to Edinburgh to take the M.B., Ch.B., and gives a very good word-picture of student life in these two Scottish universities. He was by temperament as much a soldier as a doctor, and this led him to enter the Indian Medical Service. The first part of his service was with Indian infantry and cavalry regiments of the North-West Frontier Force, and he describes the duties which fell to the lot of a regimental medical officer in the stirring and dangerous surroundings of the frontier outposts of India—the Malakand, Khyber Pass, Waziristan, these no-man's lands between Afghanistan and India which have ever been a source of trouble. Later he was transferred to Bengal and became deputy sanitary commissioner, which involved lecturing on public health in Calcutta University, but a longing for clinical work led him to apply for, and obtain, a district civil surgeoncy. In this capacity he found ample scope. As civil surgeon in charge of the headquarters hospital of the district he had to be chief operating surgeon, physician, gynaecologist, and pathologist. He gave the systematic lectures on public health and vital statistics at Calcutta University and was professor of mental diseases and professor of ophthalmology, while for eighteen months he combined the posts of first surgeon at the European Presidency Hospital and superintendent of the European Asylum—a veritable medical Pooh-Bah. He kept himself physically fit by sports and games—tiger shooting, racing, steeplechasing, pig-sticking, and golf: in the last-named he played in the golf championship of Northern India.

The author commanded general hospitals in Mesopotamia and Palestine during the 1914-18 war, and in 1919 he left the I.M.S. to join the R.A.F., which was starting its own medical service. He began by studying the special medical problems of aviation and rose to be Air Vice-Marshal and Director of Medical Services, R.A.F. In 1930

he became secretary of the Industrial Health Research Board of the Medical Research Council. In 1938 he was made Rector of St. Andrews University. Though written in lighter vein and for the general public, his book will be found full of interest by medical men, especially those who by force of circumstances stay at home and do not know the wide horizon, the golden land of opportunity which awaits members of the profession who go out to the Empire to practise.

PHYSIOPATHOLOGY OF THE EXTRAHEPATIC BILIARY PASSAGES

Fisiopatologia del Hepato-Colédoco: Colangiografia Operatoria. By Pablo L. Mirizzi. (Pp. 279. No price given.) Buenos Aires: "El Ateneo."

The reviewer has not been able to find an existing English equivalent for the compound term "hepato-colédoco," which neatly suggests the physiological reciprocity between the hepatic duct (hepático) and the common bile duct (colédoco). In this handsomely produced and lavishly illustrated monograph the author, who is professor of clinical surgery in the University of Córdoba (Argentina), has summarized his views and experiences of the technique of radiographic visualization of the extrahepatic biliary passages by the direct injection of contrast media. The first chapter deals briefly with the anatomy of the bile passages, while the second is a rather more detailed account of their physiology, with particular reference to the hepatic and common bile ducts. In Chapter III are discussed the advantages and disadvantages of operative cholangiography and the techniques of injection and radiography. The results of the author's own experiments on thirty-seven dogs are described in the following chapter. The contents of further chapters are well indicated by their titles: V, The Normal Biliary Tree; VI, Odditis (an exhaustive account of this condition); VII, Stenosing Pancreatitis; VIII, Lithiasis (of the hepatic and common bile ducts); IX, Anomalies (of the hepatic and common bile ducts). The final and tenth chapter is devoted to a consideration of errors of technique. The bibliography is conspicuous by a complete absence of references to British sources, though French, German, and North American authors are freely cited.

Notes on Books

Of Sir COMYNS BERKELEY'S services to gynaecology, and so to the welfare of our women patients, not the least is his textbook, *Gynaecology for Nurses and Gynaecological Nursing* (eighth edition, Faber and Faber, 8s. 6d.). It contains just about as much information as can be written down profitably, as an accompaniment to experience. All that a nurse need know seems to be there, including specimens of G.N.C. examination questions, which sometimes, however, seem to ask for more than a nurse need know. The price is low, the format comfortable, the style clear, with helpful paragraphing. Though no two gynaecologists would agree on every detail, Sir Comyns Berkeley has steered through the whirlpools of controversy, and has always left room for an individual gynaecological surgeon's orders to his nursing staff. The one-page chapter on "The Bearing of the Nurse" is a gem. The tabulated systems of nursing are clear and reliable. Could the index be a little fuller next time, including, for instance, "Fistula"?

The *Proceedings of the Cardiff Medical Society* for the session 1940-1 have been published by William Lewis (Printers) Limited of Cardiff. They include an article on blood transfusion by Dr. R. Drummond, regional blood transfusion officer for Wales; reports of clinical meetings and discussions; and the text of Sir Thomas Lewis's annual address to the society on April 8, 1941, entitled "Caleb Hillier Parry, M.D., F.R.S. (1755-1822): A Great Welsh Physician and Scientist." Sir Thomas described Parry as a man who in the fullness of his career was an eminent physician of Bath, a philosophic writer in advance of his times, a progressive agriculturist, and a clinical scientist of outstanding merit. He quotes from the clinical description that was Parry's masterpiece—the first account of the disease exophthalmic goitre, written in 1786.

Preparations and Appliances

AN IMPROVED LARYNGOSCOPE

Prof. R. R. MACINTOSH, D.M., D.A., writes from the 'Nuffield Department of Anaesthetics, Oxford:

The laryngoscope illustrated incorporates an epiglottis retractor and an improved method of illuminating the larynx.

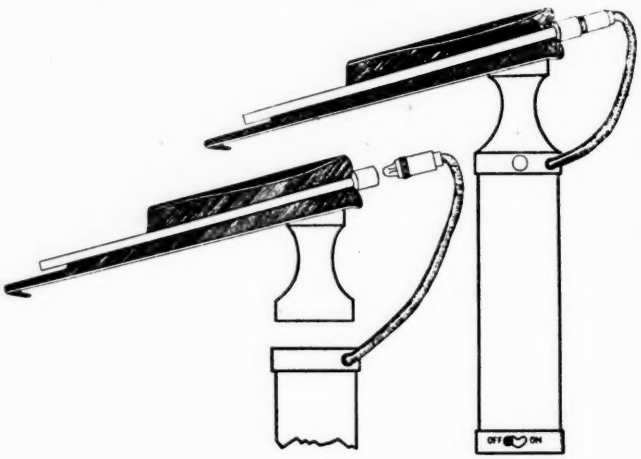

FIG. 1

Epiglottis Retractor.—When the blade of a laryngoscope is inserted the epiglottis is at first pushed backwards over the laryngeal entrance (Fig. 2a). Every anaesthetist has on occasion had difficulty in everting the epiglottis so as to expose the larynx. When the new blade is used the metal elevation passes over the epiglottis, which then lodges in the notch (Fig. 2b). When the blade is withdrawn slightly the epiglottis is everted (Fig. 2c) and the larynx comes into view.

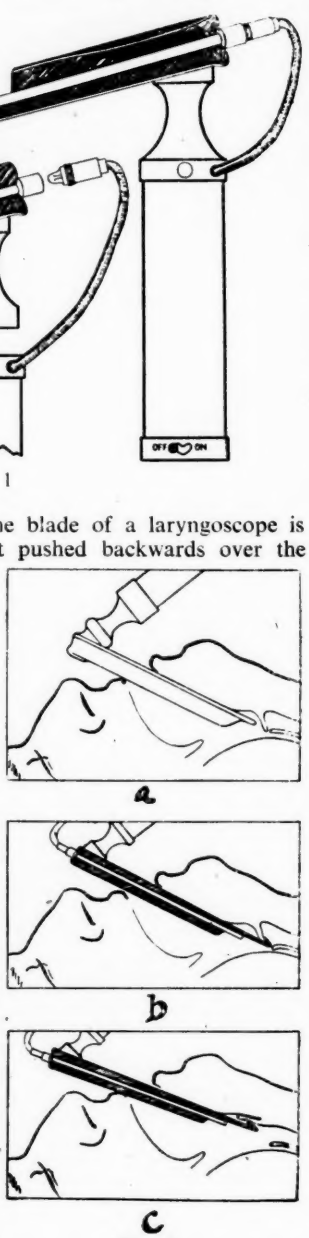

FIG. 2

Illumination.—The orthodox illumination consists of a small electric bulb attached to the blade. This bulb is difficult to sterilize, expensive (6s. 6d.), fragile, and if it breaks in the presence of ether vapour or cyclopropane might cause an explosion. In the new laryngoscope the source of light is an ordinary robust torch bulb (price 1s.) attached not to the blade but to the battery in the handle by a flexible lead. From the bulb the light is carried to the field of operation by a pencil-shaped rod of curvelite fixed to the blade. The blade is readily detached from both bulb and handle and after use is washed and boiled.

I am indebted to Mr. R. Salt, technician to this department, for his help in making the original model. The laryngoscope can be obtained from either Medical and Industrial Equipment Ltd., of 12, New Cavendish Street, London, W.1, or Vann Bros., Ltd., 63, Weymouth Street, London, W.1.

BRITISH MEDICAL JOURNAL
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REFRACTORY ANAEMIA

Recent improvements in the treatment of blood diseases have brought into prominence a group of cases in which the anaemia does not respond to treatment by iron or liver, although no simple cause for anaemia such as haemorrhage, toxaemia, or neoplasm can be detected. One of the first things to be suspected in such a case is leukaemia of the leucopenic type. In the early stages of subacute myeloid leukaemia neither spleen nor lymph glands may be palpable, and the presence of immature cells in the blood stream may be difficult to establish with certainty. In such cases the diagnosis can be made by sternal puncture, for the bone marrow is always infiltrated. In subacute lymphatic leukaemia the sternal puncture is not always pathognomonic,[1] but if at the same time there is no enlargement of lymph glands this diagnosis can for all practical purposes be excluded. An obscure haemolytic anaemia is another possibility, but this will be revealed by persistent reticulocytosis and an increased excretion of pigments in the urine and the faeces. In severe hepatic disease there may be a megalocytic anaemia, but the evidence of liver damage is usually obvious. Myxoedema is another condition in which pernicious anaemia may be closely mimicked. When all these possibilities have been discarded there remains a residuum of cases in which the common factor is anaemia which resists all treatment except transfusion. Bomford and Rhoads[2] have had the unique experience of studying sixty-six cases of this type at the Rockefeller Institute, and their findings are of wide interest.

The difficulties of nomenclature are considerable, and they prefer to call these cases "refractory anaemia." They can be subdivided, according to the appearances of the bone marrow, into four groups. In the first group the marrow is cellular and relatively mature; erythropoietic cells usually predominate over leucopoietic cells; the authors include the achrestic anaemia of Israels and Wilkinson[3] in this group. The second group is the classical aplastic anaemia in which the marrow is fatty and few haemopoietic cells are present. The third group is the most difficult and disputed: the marrow is cellular with a predominance of cells somewhat resembling lymphocytes; the other tissues, however, show no evidence of lymphatic infiltration, and it is believed that the cells in the bone marrow are atypical nucleated red cells. In the fourth group there are fibrosis, sclerosis, and giant-cell hyperplasia of the marrow. The distinction between these groups is not hard and fast, and successive biopsies show that the marrow may pass from one stage to another. Moreover, the changes in the rest of the body differ little in the four groups. Extramedullary haemopoiesis is greatest in the sclerotic type, but it occurs to some degree in all types; haemosiderosis and degeneration of liver cells may also be present in all. There is evidence that exposure to a single haemotoxin—benzol—may produce all these changes except possibly sclerosis of the marrow. Myelosclerosis differs also in the normal platelet count and the strong tendency to enlargement of the liver and spleen. Many haematologists, indeed, would regard myelosclerosis as akin to Hodgkin's disease, and of a different nature from the other three groups, which can be regarded as toxic-aplastic reactions of the marrow. The position is complicated, however, inasmuch as benzol poisoning may lead to leukaemia, and refractory anaemia may sometimes be a phase in the development of the same process.

Clinically all these refractory anaemias present much the same picture of anaemia, leucopenia, and, with the exception noted, thrombocytopenia. The colour index is usually normal or above normal, and in cases of long duration a considerable megalocytosis may develop. One of the most interesting discoveries is that the breakdown of blood is often accelerated in these patients, pigmentation of the skin and haemochromatosis are frequent, and transfused blood may be destroyed more rapidly than normal. The disease occurs at all ages, and remissions are not unusual. More than a third of the Rockefeller patients were known to have been exposed to potentially toxic agents, of which benzol and its synthetic derivatives, *x* rays, and radio-active materials were the most frequent. Volatile insecticides and paraphenylene diamine hair-dyes are new items in this sinister catalogue. The authors regard removal from such potentially toxic substances as the most important element in treatment; in early cases it is often curative. In some cases the toxin may be endogenous, a suggestion supported by Rhoads's earlier work on the effect of indole. Idiosyncrasy must usually be present for so severe a reaction to occur. There is both experimental and clinical evidence that defective diet may be one factor responsible for it. The proof that defective liver function is another factor is even stronger. Both biochemical and anatomical signs of liver damage can be found in many of the cases. The authors' working hypothesis of the aetiology of refractory anaemia is that "the disorder is due to a conditioned susceptibility to toxic substances, usually exogenous or endogenous aromatic hydrocarbons, associated with hepatic dysfunction, a failure of biochemical mechanisms of detoxication, and the circulation of haemolytic substances, and that these haemolysins cause either an abnormal form of haemolysis and thus an abnormal reaction in the marrow, or that they destroy both circulating red cells and developing cells in the marrow, thus producing hypoplasia or other abnormal forms of marrow."

Apart from transfusion the only remedy which seemed to have an effect was baker's yeast in large doses. In very rare cases, where haemolysis is clearly excessive, splenectomy may be contemplated, though it is in no sense a cure. Prevention must remain the most important weapon. This long paper is of more than passing

[1] *Acta med. scand.*, 1941, Supp. 112.
[2] *Quart. J. Med.*, 1941, **10**, 175, 235.
[3] Ibid., 1936, **5**, 69.

interest when so many of our workpeople are exposed to the hazards of potentially toxic substances in war industry. Trinitrotoluene[4] produces this same combination of liver damage and aplastic anaemia in the unfortunate few who possess an idiosyncrasy for it, and those who are working on the problems of prophylaxis and early detection of such idiosyncrasy will learn much from the ideas and technical methods which Bomford and Rhoads have developed.

THE MILK (SPECIAL DESIGNATIONS) REGULATIONS, 1941

The Minister of Health, in the exercise of his powers under the Food and Drugs Act, 1938, has recently issued as a provisional Order the Milk (Special Designations) Regulations, 1941. The Order permits local authorities to grant licences to use the special designation "pasteurized" in respect of milk which has been heated at a temperature of not less than 162° F. for not less than fifteen seconds in apparatus of a type approved by the authority. The use of the process—for long known as high-temperature short-time pasteurization (H.T.S.T.)—is therefore now officially sanctioned. The widespread employment of the phosphatase test by authorities controlling licensed pasteurization plants has in the last two or three years shown that in an alarming number of cases the terms of the licences have not been observed. This, it is to be noted, applies to the holder-pasteurization system of heating at 145° F. for thirty minutes, which alone until now has been officially permitted. It is well known that this process carried out in well-constructed and properly controlled apparatus can be relied upon to ensure the freedom of milk from living pathogenic organisms, to cause minimal damage to the nutritive and physical properties of milk, and to improve the keeping quality. This process, based on careful laboratory experiment and proved by years of practical experience, is one which is well adapted to proper control by the licensing authorities. The flow of milk through the apparatus is required to be totally arrested for a period of not less than thirty minutes at a temperature of not less than 145° F. Both time and temperature afford ample margins of safety. Nevertheless, the control of apparatus designed to conform to the excellent official requirements demands knowledge, skill, and diligence from the representatives of the licensing authorities. That these have not always been forthcoming has been revealed by the phosphatase test.

What, then, is the reaction to the new Order? The holder type of plant occupies much space, requires much metal, is difficult to clean, and is necessarily rather inflexible in operation. Existing plants are wearing out and must be replaced, and the difficulties of operation imposed by war conditions are great. But the safety of the milk supply is more than ever necessary. These considerations have avowedly prompted the Minister to sanction the use of apparatus which occupies little space, is easy to clean and maintain, and is notable for its flexibility—all of which are desirable attributes in wartime. Further, there is evidence that the H.T.S.T. process disposes efficiently of pathogenic organisms and that changes in the physical, chemical, and nutritive properties of the milk are, as in the holder process, minimal. The essential difference between this and the holder system is that at no time is the flow of the milk actually arrested. Moreover, the margins of safety, though similar on a relative basis, are less in terms of absolute time and temperature, and demand great precision in control. The Order requires that the apparatus shall be thermostatically controlled, fitted with an automatic device to divert milk which has not been properly heated, and furnished with such indicating and recording thermometers as the licensing authority thinks requisite. The licensing authorities must also decide on the suitability of the apparatus and thermometers used.

Much that is not categorically stated is laid on the licensing authorities, and it is clear that the H.T.S.T. process demands a well-informed and technically minded inspectorate. It will be necessary for them to recognize the lag of thermometers in responding to temperature changes, to bear in mind the mechanics of the flow of liquids through pipes, tubes, or their equivalents—the so-called "holder" section—to ensure the minimum holding time of fifteen seconds, and to be sure that the rate of flow of the milk through the machine, which determines the holding time, does not vary. Thermometers and recording apparatus must be checked against standard thermometers, and the considerations governing their positions in the plant must be appreciated. Great advances in the design of plant and control apparatus have been made in recent years and some of the essential parts of the newer apparatus are familiar to many, as they have for long been incorporated in holder machines. This, coupled with a substantial volume of satisfactory experience of the practical working of H.T.S.T. machines here and in America, goes far to allay any anxiety which may be felt as to the capacity of local authorities to implement the new Order.

The Order is provisional and the times are abnormal, but the safety of the milk supply must be assured. The advantages of the new system may well outweigh any apparent difficulties of administration and lead to important changes in the milk industry. Local authorities will no doubt take the steps necessary to dispel the doubts of those who maintain that licensing of plants should be in the hands of the central authority.

[4] *British Medical Journal*, 1941, **2**, 509.

DIABETOGENIC ACTIVITY AND GROWTH

In 1937 F. G. Young[1] discovered that a short period of injections with anterior pituitary extracts induced in dogs a permanently diabetic condition—a condition he calls pituitary-diabetes. Later it was shown that the treatment caused changes in the islet tissue of the pancreas.[2] The findings served to explain the glycosuria which H. M. Evans and his colleagues[3] found in some of their puppies treated with pituitary growth-promoting extracts, an observation not particularly stressed at the time and apparently not further investigated. In an important paper published elsewhere in

[1] *Lancet*, 1937, **2**, 372.
[2] Richardson, K. C., and Young, F. G., *Lancet*, 1938, **1**, 1098.
[3] *Proc. Soc. exp. Biol.*, N.Y., 1931-2, **29**, 857.

this issue Young has now brought forward evidence relating the growth-promoting and diabetogenic actions of pituitary extracts. The chemical properties of the two active extracts are similar, and Young's diabetogenic extracts have contained growth-promoting activity. In his first experiment he finds that injection of a pituitary extract which has diabetogenic activity in adult dogs did not produce glycosuria in puppies, even when given in more than six times the dose active in the adults; there was, however, considerable acceleration of increase in body weight. One of the puppies eventually developed glycosuria at a weight of 20 kg.; this is persisting at the time of writing. In a second series of experiments extracts which are diabetogenic in normal adult dogs and similar extracts which have lost their diabetogenic activity were injected into pituitary-diabetic dogs. These extracts were known to contain pancreotrophic activity—that is, they cause an increase in the islet tissue and insulin content of the rat's pancreas. The results were not completely consistent, and the variations in response probably depended on the amount of undamaged islet tissue surviving in the pancreas of the pituitary-diabetic dogs. In some cases the severity of the diabetic condition was increased; in others it was ameliorated. These contrary results appear to be bound up with the nitrogen metabolism of the dog: when the diabetes is alleviated there are nitrogen retention and increase in body weight; when the condition is intensified there are increased nitrogen loss and fall in body weight. Growth-hormone preparations are known to induce nitrogen retention, and it is probable that this action is mediated by the islets of Langerhans.

An important aspect of the experiments lies in the clues they give to some of the factors in clinical diabetes. The majority of adult diabetics are over weight, and White has found that many diabetic children are above the average height. There is evidence that children have greater amounts of islet tissue in proportion to body weight than have adults, and if this condition holds in the dog the relative resistance of the puppies to diabetogenic extracts may be explained, the greater amount of islet tissue being sufficient for normal blood-sugar regulation, even in the presence of pituitary diabetogenic activity. Young puts forward the theory that slight pituitary overaction in the child may cause compensatory islet hypertrophy with nitrogen retention and growth; in the adult the same may occur, the stimulus increasing body weight but not being enough to cause skeletal changes. It is then suggested that the islet tissue may not be capable of maintaining this hypertrophy, so that lesions become predominant and the symptoms of diabetes follow. These suggestions and the evidence for them are considered in greater detail in the discussion in Young's paper, but enough has been said to demonstrate the possibilities of the hypothesis. Many cases of diabetes may therefore be caused by pituitary - pancreas imbalance rather than by primary pancreatic lesions. This suggestion obviously affords scope for future experiments, and it is to be hoped that Young will be able to continue his researches not only into the mechanism of production of diabetes but also into the vexed question of the nature and activity of the growth hormone. It may be noted that he is careful to refer to "growth" in inverted commas, as his data at present only refer to changes in body weight, neither the components of this weight increase nor the skeletal changes having been determined in the present preliminary statement.

AETIOLOGY AND TREATMENT OF OSTEO-ARTHRITIS

In most cases osteo-arthritis is a degenerative process set up by repeated small injuries, often incurred during work. Once the cartilage has been even slightly injured the degenerative process progresses and causes steadily increasing disability; but in a large number of cases pain is not a conspicuous feature, and in consequence treatment is not seriously undertaken until the removal of the more obvious causes by change of occupation is likely to be of little effect. Magnuson[1] has carried out extensive experiments on dogs to investigate the changes that take place after slight injury to the cartilage and the mechanism by which they are produced. As an outcome of this work he has devised, and successfully performed, an operation in the human subject to which he has given the name "joint débridement." He has demonstrated that local areas of roughened cartilage may result from superficial injury which gradually progresses more deeply; or the degenerative process may begin in the matrix and gradually lead to fissuring and degeneration of the articular surface. Continual friction by the use of the joint leads to further damage round the original site and on the surface of the opposed cartilage. Magnuson has found it difficult to explain the causes of proliferation of bone round the edges of the joints—an important cause of limitation of the range of movement and often of pain—but he does not refer to the work of Corbin[2] at Stanford University, who obtained some interesting results by severing the lumbosacral nerve roots containing afferent fibres from the hip-joints. The resulting excessive range of movement and abnormal position of the joint led to erosion and fibrillation of the cartilage and to enlargement of the head of the bone and the acetabular cavity, apparently with the object of giving additional support to the limb. Pearson in 1928 produced evidence that degenerative changes take place in the posterior root fibres, as a result of arteriosclerosis affecting the column of Goll, the ability to perceive vibratory stimuli being thus diminished; it is suggested that the influence of arteriosclerosis in osteo-arthritis is exerted in this way and not directly through the blood supply of the joint, which Keefer and Myers have shown is not affected in proportion to the severity of the arthritic changes.

The operative procedure devised by Magnuson is to shave away the roughened areas completely and to remove all exostoses which may give rise to friction and interfere with the normal movements of the joint. The roughened surface being thus removed, the progress of the disease is arrested or at least delayed; the denuded areas become covered with fibrocartilage, which serves as a satisfactory substitute for the normal hyaline cartilage. Careful choice of patients is important; the full co-operation of the patient is essential. Special attention must be given to movement of the joint: this should be started on the fourth day after the operation and carried out under the close supervision of the surgeon. Magnuson has operated on sixty-two cases and has achieved good results in sixty; in the remaining two cases the patient did not co-operate and did not remain under his control. Although the number of cases is too small for exact conclusions to be drawn from this experi-

[1] *Surg. Gynec. Obstet.*, 1941, **73**, 1.
[2] *Arch. Surg.*, Chicago, 1937, **35**, 1145.

ence, the results appear to justify further trial in suitable cases of this distressing complaint. The time since operation in Magnuson's cases has varied from sixteen years to six months: it is obvious that if the operation is to be regarded as a success relief from symptoms, even if not permanent, should at least last for a period of years. It is probable that the best results will be obtained only in comparatively young subjects with clear evidence of repeated traumata as a cause, and that when there is evidence that arteriosclerosis is a contributory factor the results are less likely to be satisfactory.

CLASSIFICATION OF CROUP

Gilbert, Meyersburg, and Silverberg,[1] in analysing a series of 226 cases of croup admitted to the Kingston Avenue Hospital, Brooklyn, New York, call attention to the great decrease in the incidence of diphtheritic croup, whilst the number of cases of non-diphtheritic croup remains about the same. Before the use of diphtheria prophylactic and antitoxin 60% of the cases were diphtheritic, but in the series under review observed during one year the incidence of diphtheria was only 7%. The authors apparently assume that this remarkable change in incidence is due entirely to protective immunization, for they make no comment on the possibility that other factors may also be concerned. The analysis is therefore chiefly related to the non-diphtheritic group, for which a varied and consequently confusing nomenclature has evolved. The authors propose the following classification: (1) diphtheritic croup—(*a*) diphtheritic obstructive laryngitis, (*b*) diphtheritic obstructive laryngo-tracheitis, (*c*) diphtheritic obstructive laryngo-tracheo-bronchitis; (2) acute catarrhal laryngo-tracheitis; (3) supraglottic oedematous obstructive laryngitis; (4) subglottic obstructive laryngitis and tracheitis—(*a*) subglottic *exudative* obstructive laryngitis and tracheitis, (*b*) subglottic *oedematous* obstructive laryngitis and tracheitis; (5) acute obstructive laryngo-tracheo-bronchitis; (6) unclassified, due to allergy, foreign body, and chemical irritants. For diphtheritic croup the authors recommend in general 20,000 units of antitoxin intramuscularly and 10,000 units intravenously. Laryngoscopic suction is employed when it appears indicated. In the severe form of diphtheritic obstructive laryngo-tracheo-bronchitis tracheotomy is required and suction is carried out by passing a bronchoscope through the tracheotomy wound. The two patients with such condition in the series treated in this way both recovered.

Turning to the large non-diphtheritic group the authors draw special attention to the supraglottic oedematous obstructive laryngitis, in which the swelling affects the epiglottis and aryepiglottic folds. Tracheotomy is indicated in preference to intubation, for the swollen mucous membrane overlaps the upper end of the intubation tube and blocks the airway. All the six patients in the series treated by tracheotomy recovered. The authors believe that supraglottic and subglottic oedema rarely, if ever, occur together. For the subglottic obstruction laryngoscopic suction is recommended, and they advise tracheotomy in preference to intubation in all cases in which suction is not sufficient to provide relief. Acute obstructive laryngo-tracheitis and acute obstructive laryngo-tracheo-bronchitis must be distinguished from pneumonia by the physical signs indicating obstruction. Acute obstructive laryngo-tracheo-bronchitis, however, has a high mortality, but is treated on the same lines as the other forms of croup, in which the prognosis is good. The authors have very little information to offer on the bacteriology or chemotherapy of the conditions discussed.

[1] *Arch. Otolaryng.*, Chicago, 1941, **34**, 281.

SOLAR URTICARIA

In contradistinction to sunburn, which is solar erythema and very common, urticaria as a result of exposure to sunlight is very rare. Several cases, however, have been described, the first of which appears to have been that of Duke in 1923. He studied this case in some detail and suggested the name "urticaria solaris" for the condition. His patient was a woman aged 43 who had been affected four years. Duke was able to reproduce the lesions by sunlight filtered through colourless or violet glass and also by electric light. *X* rays were ineffective. He thought that the spectral region responsible was the visible portion together with the far red and infra-red. A good many cases have been described since that time and rough attempts have been made with filters of various colours to determine the part of the spectrum which is to blame for the manifestation. But the use of filters is full of pitfalls for the unwary, for many filters have broad transmission bands well outside the spectral range that their colour suggests. The one readily available "cut-off" filter which can be relied on is ordinary window glass. It absorbs almost all wave-lengths shorter than about 3,200 Angstrom units—that is, almost all the ultra-violet region. Dr. Arnold[1] of Hawaii had the opportunity of studying a case in some detail in a young man of 26 who, when he came under observation, had been subject to the condition for some five years, although owing to the patient's early departure the investigations could not be completed. His reaction to sunlight filtered through window glass was just as severe as to direct sunlight, but he was not at all sensitive to light from the air-cooled quartz mercury vapour lamp. He was also very little sensitive to photoflood lights, which include much red and infra-red, or to the carbon arc lamp, which includes much violet and ultra-violet. These observations seem extremely difficult to explain. More information was obtained from the study of filter data. To epitomize the results of these investigations, it may be stated that the maximum response was elicited from radiation of wavelength from 3,800 to 5,000 Angstrom units, but all the same the four mercury lines in and adjacent to that region must be ineffective, or there would be a response to the mercury vapour lamp. No response at all was obtained from irradiation through the Wratten green gelatin filter of thirty minutes' sunlight. This filter transmits not only green but the entire infra-red portion of the spectrum, and these regions must therefore be exonerated. It appears probable that the effective rays are to be found in the blue and violet regions, but their exact position cannot be clearly defined.

[1] *Arch. Derm. Syph.*, Chicago, 1941, **43**, 697.

At the last Court of Governors of the Middlesex Hospital Sir Alfred Webb-Johnson was elected a Vice-President of the hospital. The Court desired to recognize not only his election as President of the Royal College of Surgeons but also his invaluable services in the planning and rebuilding of the hospital, and in the raising of so large a part of the sum required for the reconstruction scheme. This is the first occasion on which this honour has been conferred upon an active member of the honorary staff.

We regret to announce the death of Dr. Robert Dawson Rudolf, C.B.E., F.R.C.P., emeritus professor of therapeutics in the University of Toronto and consulting physician to the Toronto General Hospital and Sick Children's Hospital. Dr. Rudolf during the last war was consulting physician to the Canadian Forces in England with the rank of Colonel C.A.M.C.

REGIONAL HOSPITAL SERVICES

POLICIES OF NUFFIELD TRUST AND B.H.A.

The British Hospitals Association has issued a "Memorandum of Policy on Regionalization of Hospital Services," although the uncouth word "regionalization," as it explains, is to be dispensed with so far as possible in favour of the term "co-ordination." The memorandum was prepared before the Minister of Health's statement in the House of Commons on October 9 defining the Government's post-war policy on hospitals, but no amendment has been found necessary. The document is really a postscript, although a very substantial one, to a pamphlet by the Nuffield Provincial Hospitals Trust on "The Co-ordination of Hospital Services," which should be read first.

The Nuffield Trust, founded two years ago, has for its object the co-ordination on a regional basis of hospital and ancillary medical services throughout the Provinces, Scotland, Wales, and Northern Ireland. For the London area, so far as voluntary hospitals are concerned, the King Edward's Hospital Fund serves as a central financial organization. The Voluntary Hospitals Commission, under Lord Sankey, recommended the division of the country into regions, with a council in each region to correlate hospital work. The necessity was recognized for co-ordination not only between voluntary hospitals themselves, but between voluntary and municipal, if overlapping was to be avoided, the best use was to be made of available accommodation, and consultation was to take place before new services were started. With these considerations in mind Lord Nuffield created and financed the Trust. During the last eighteen months preliminary conferences have been held in many large centres, and a number of regional or divisional councils have been formed or are in process of formation.

General Medical Policy of Nuffield Trust

A statement by the Medical Advisory Council of the Nuffield Trust—a council which comprises twenty-four leading representatives of medicine under the chairmanship of Sir Farquhar Buzzard—is embodied in the Trust pamphlet. The Council points out that the problem facing each region is, while centralizing the more expensive and specialized methods of investigation and treatment at the larger hospitals, to ensure that these are accessible in case of need to every practitioner and patient within the region. The small and scattered hospitals must be linked up, by visits from the consulting staff and in other ways, with the "key" hospital (meaning by the latter teaching hospitals or, in divisions where there are no medical schools, large non-teaching hospitals). Such linkage will be one method of bringing the general practitioner into closer contact with the "key" hospital.

The distribution of consultants and specialists in the new or future "regions" has been unequal. In some areas it may be advisable for consultants, while nominally on the staff of the "key" hospital, to reside in an outlying area and serve a group of small hospitals. Perhaps medical appointments may be made, not to individual hospitals, but to a region or group of hospitals within a region, so that each member of the staff may eventually carry out the work for which his abilities and experience most suit him, whether general consulting practice, one of the specialties, teaching, or research.

The findings of the Interdepartmental Committee on Rehabilitation, published in 1939, have the approval of the Medical Advisory Council, but fracture services in themselves are not considered to be enough; what is needed is an "accident service" organized regionally to treat not only fractures but lacerations and contusions, burns and scalds, and sepsis as a result of injury.

As for pathological services, these in the large teaching hospitals leave little to be desired, but in the country as a whole they fall far short of requirements. The Council urges that existing laboratory facilities should be co-ordinated on a regional basis, which would increase their efficiency in various ways, enabling any laboratory within the region to have in a consultative capacity the services of a highly skilled bacteriologist, morbid anatomist, or other expert. It sets out certain conditions to be secured in the administration of pathological services, the principle being that all such work should be done by pathologists attached to public health laboratories, hospitals, or university departments; that all clinical pathology should be done by pathologists working in hospital laboratories; and that in each region or division there should be at least one public health laboratory concerned mainly with epidemiological work and co-operating in that field with medical officers of health and general practitioners.

How Regions are to be Determined

The British Hospitals Association in its complementary memorandum states its entire agreement with the principles of co-ordinated hospital services as described by the Nuffield Trust. The Association has had its own regions and regional committees, but to avoid confusion it is renaming them "areas," their boundaries to be so far as possible coterminous with those of the "divisions" or parts of regions through which co-ordination will be developed locally. Close contact between the B.H.A., the Trust, and King Edward's Hospital Fund has been ensured by arrangements for representatives of each body to sit on the councils of the others.

In proceeding to effect co-ordination the local area committee of the B.H.A.—which represents voluntary hospitals only—if it feels that local conditions are favourable, will invite representatives of the local authorities to a preliminary conference and proceed to a detailed examination of a scheme, not overlooking contiguous areas. Alternatively the Nuffield Trust may, after consultations, take the initiative of calling a preliminary conference to which representatives of both voluntary hospitals and local authorities will be invited. The voluntary hospitals as such will from time to time have a policy or unanimous view to express, and this can be done through the area committees; the regional council consists of municipal as well as voluntary representatives.

It is fully recognized that it is not competent for voluntary hospitals alone to determine areas; the views of local authorities are of at least equal importance. Nor must areas be considered as surrounded by a Chinese Wall or unbreakable barriers; a region or division is merely a unit formed after taking into consideration a number of factors, such as the nature of the hospital services generally available. It is not desired to interfere with the freedom of the patient in his choice of doctor or of the doctor in his choice of hospital or consultant. The unit must be formed naturally, and in its formation there will be no compulsion on a particular hospital.

There are hospitals which are apprehensive of co-ordination as threatening their existence or development.

"... Co-ordination does not mean the domination of the unit by one centre; it does not mean a concentration of all the specialist services at, for instance, a teaching hospital and the reduction of all other hospitals in the region to a secondary standing; but on the other hand it does mean the improvement and the maintenance of an adequate standard of services in the region or division."

This may be accomplished in some cases by concentrations of services, in others by dispersal.

Again, the regional and divisional councils are essentially advisory bodies, or are executive only to such extent as powers are given to them unanimously by their constituents. Co-ordination, in fact, is a reciprocal matter between voluntary hospitals and agencies on the one hand and local authorities on the other. It calls for mutual understanding and confidence and a pooling of knowledge and facilities.

H. R. Russell and R. C. Page (*Amer. J. med. Sci.*, 1941, **202**, 355) point out that, as vitamin K belongs to the group of fat-soluble vitamins, it should be absorbed through the skin. Accordingly they applied 10 milligrammes of synthetic vitamin K analogue in an ointment base to a series of newborn infants. A single application was found to be effective in preventing hypoprothrombinaemia.

AWARDS FOR GALLANTRY

The awards of the M.B.E. (Civil Division) to Dr. William Louis Murray Bigby, assistant medical officer of health for civil defence, Southampton, and to Dr. John Findlay, doctor in charge, first-aid post, Civil Defence First-aid Post Service, Peterhead, and the B.E.M. (Civil Division) to Mr. R. A. Gow, caretaker, Civil Defence First-aid Post Service, Peterhead, are announced in the second *Supplement* to the *London Gazette* dated December 12. The announcements read as follows:

Dr. BIGBY: Dr. Bigby has been on duty throughout the period of air raids on Southampton. He has worked long hours helping to extricate trapped people, and on several occasions has entered wrecked buildings in order to relieve the sufferings of the injured. He has shown courage and qualities of leadership without regard to his own safety."

Dr. FINDLAY and Mr. GOW: "A high-explosive bomb demolished a building, and members of a first-aid post were injured and trapped. Dr. Findlay was thrown to the floor and injured, but despite this, at grave risk to himself, he crawled under the loose debris and gave injections to three casualties. He then organized the removal of the post to a temporary site, where he again took charge. Dr. Findlay showed qualities of leadership, courage, and devotion to duty, and in his work of rescue was helped by Mr. Gow, who, although badly shocked, courageously worked with the doctor for two hours, searching for the injured men."

Reports of Societies

WARTIME RATIONING AND CHILDREN'S HEALTH

At a meeting of the Section for the Study of Disease in Children (Royal Society of Medicine) on November 28, with Dr. A. G. MAITLAND-JONES in the chair, a discussion took place on the effects of wartime rationing on child health.

Dr. E. M. WIDDOWSON mentioned a dietary survey carried out during the years 1935-9 on 1,000 individual middle-class children, the data of which had since been re-analysed to show the effects that rationing must have had on the diets of these children. The pre-war consumption of most foods, whether now rationed or unrationed, was found, as might be expected, to rise with increasing age. A comparison of the intake before the war of foods now rationed with the actual rations to-day gave an idea of what the changes must have been. Up to the age of 6 children with the green ration book got half the adult allowance, and from then onwards the full adult ration. Up to the age of about 8 children were just as well off in respect of butcher's meat as before the war, but boys of 15 before the war were eating about three times as much meat as they were now allowed. The average boy was also eating before the war about twice as much sugar as now. Butter was much reduced in the child's wartime dietary, but the position was different with regard to cheese, which was eaten by only a small proportion of children in pre-war times. If the child below 8 was eating the whole of his rations he was just as well off as before the war, except for butter; the child over the age of 8 was not as well off, and adolescents had had to make a big change in their dietary habits. All this was on the assumption that the rationing system was rigidly followed, whereas, of course, in the ordinary family it would not be, the older children probably receiving larger helpings of pudding made with the family's sugar and jam ration, and in boarding schools for children of 14 to 18 the effect of rationing was probably most markedly seen. Milk had only just begun to be severely restricted, but children were in a priority group, and with the help of school milk might get, until leaving school, even more milk than they got before the war. The children who suffered most were those who left school at 14, when calcium requirements were at their maximum. The availability of vitamin C was reduced, not on account of rationing but because of the scarcity of fruit. Scurvy, however, did not seem to have appeared.

Recognition of Dietary Deficiency

Dr. D. C. WILSON said that it was important to appreciate the difference between examination for signs of malnutrition carried out during routine school inspection and the use of growing children as indicators for the detection of signs of dietary deficiency within a community. During medical inspection the state of nutrition was assessed according to the standards laid down by the Board of Education. Such examination was useful in drawing attention to the many different causes in home and school life which might adversely affect the child's well-being, and thus permitting the application of the appropriate remedy. For the early detection of specific dietary deficiency within any group special tests were necessary, and these, applicable under wartime conditions in English schools, were described.

Dr. HELEN MACKAY said that it must not be supposed that because a child's ration had been calculated he would get it, and that there was no need to look for deficiency disease. Distribution was often far from ideal. A great deal depended on whether the people who looked after the children knew the best substitutes for food in short supply and how to use them. There was a general impression among paediatricians and in the public health services that tuberculosis had increased. One could only guess how much of this was due to the wholesale discharge of cases at the beginning of the war, how much to the consumption of unboiled tubercle-infected milk by evacuated city children accustomed to pasteurized milk, and how much to deficient diet. She emphasized the importance of looking for objective evidence in deficiency diseases; the subjective classification in many public health reports seemed utterly useless. There was some increase of rickets last winter, but she had not seen any signs of scurvy in her clinic, nor any increase in angular stomatitis or conjunctivitis. The proposal for well-balanced school meals should be supported. Something ought also to be done for mothers of young children, who probably suffered from giving away their rations.

Vitamin C Deficiency in Children

Dr. W. W. PAYNE said that children at a base hospital in the spring of 1941 were examined by a single saturation test and found to be uniformly deficient. The hospital diet was very inadequate in vitamin C and was estimated to give only 6 mg. of ascorbic acid a day with average helpings of vegetables. Supplements of 50 mg. ascorbic acid daily for fourteen to twenty-one days failed to saturate. On giving the full saturation dose (50 mg. ascorbic acid per stone daily), it was found that only fourteen out of twenty-seven became saturated within three days. In seven of these the failure to saturate was probably due to the illness. Thus six of the twenty-seven children tested were very deficient in vitamin C, having an approximate deficit of 1,000 mg. of ascorbic acid. Once these children were saturated it was found that a dose between 20 and 40 mg. a day sufficed to keep them so. Certain non-febrile diseases appeared to require more ascorbic acid—for example, chorea, ulcerative colitis, and coeliac disease.

Dr. J. A. GLOVER said that the school child at the beginning of this war was in far better condition than his predecessor in 1914—bigger, better nurtured, better clad, cleaner, and more resistant to infection. It was impossible to disentangle the effects of rationing from those of many other abnormal factors which influenced wartime health and nutrition, such as evacuation, closing of schools, and shelter life. The most reliable evidence against deterioration was the opinion of the great majority of school doctors, nurses, and teachers. The decreased incidence of infectious diseases might also be regarded as evidence against deterioration. There was a temporary increase of scarlet fever and diphtheria in the last quarter of 1939, but it died away very rapidly. Tuberculosis had possibly increased to some extent, but his impression was that the incidence of acute rheumatism and chorea had somewhat decreased.

Dr. H. P. BAYON spoke of the importance of iron in the nutrition of children. The greatest trouble in practice was the weaning period, with lack of eggs and oranges and unreliable supplies of cod-liver oil. It was not enough to have the requisite iron or vitamins in the food if the food was not

easily assimilable. Palatability had to be considered along with nutrition.

Prof. A. ST. G. HUGGETT said that if the mother during pregnancy were on a short diet the child would benefit at the expense of the mother at first, but if the shortage continued the child also would be affected and show anaemia after birth. From certain records of infants born during the first six months of the present year there appeared to be some loss of weight. It was likely that infants would show less resistance to disease unless the mother's diet during lactation could be kept well up to requirements. With regard to vitamin C, ascorbic acid tablets were not a good substitute for fresh vegetables. Bread became more important with the cutting down of milk, but unless something were supplied to lubricate the bread the right quantity for the pregnant woman would not be taken, and both she and the child would suffer.

MODE OF ACTION OF CHEMOTHERAPEUTIC AGENTS

The Biochemical Society held a discussion meeting on the mode of action of chemotherapeutic agents on November 29 at the Courtauld Institute of Biochemistry, Middlesex Hospital, Prof. E. C. DODDS being in the chair.

General Principles

Dr. G. M. FINDLAY, in opening the discussion, said that chemotherapeutic action might be classified as direct or indirect. Except in the case of parasites present in the intestinal canal it was essential that the chemotherapeutic drug should be absorbed into the body, that it should penetrate to the site where the parasites were acting, and that it should not be excreted or converted too rapidly into an inert form. Time must be allowed for chemotherapeutic action and, in some cases, for the conversion of the compound from an inactive into an active form.

When once the drug and the parasite had been brought face to face three stages might be distinguished—adsorption, interference with metabolism, and death or such injury to the parasite that it was destroyed by the phagocytes of the host. An adsorbed chemotherapeutic drug might prevent an essential food factor from being absorbed, or it might cause a breakdown in metabolism by combining with a specific substrate or by competing with an essential cell metabolite for an enzyme or coenzyme. One break in the chain of metabolic reactions might rapidly give rise to others. Specific immune serum and sulphapyridine did not compete for the same receptor group in the pneumococcus and might therefore enhance one another. Parasites might be killed in the body without the aid of phagocytes, but usually when a parasite had been damaged it was destroyed by the normal defence mechanism of the host.

Indirect action produced such changes in the environment that parasites could no longer grow. Physical changes might prevent growth, the temperature or the *p*H reaction be altered, the formation of immune bodies stimulated, or the character of the cells altered, as in the treatment of gonococcal vulvovaginitis in children with oestrogen preparations. The highly specific action of certain drugs, and the no less specific reactions of certain closely allied parasites, could be explained by postulating that after adsorption of the compound at the parasite-solution interface the nature of the interference with the metabolism of the parasite depended on what groupings in the molecule of the compound came within the influence of other acceptor groups in the parasite: there was thus a multi-point action.

Penicillin

Prof. A. FLEMING, continuing the discussion, said that in 1929 he had applied the name "penicillin" to an antibacterial substance of unknown constitution elaborated by *Penicillium notatum* when grown in ordinary bacteriological media or in a modified Czapek-Dox medium. The action was mainly bacteriostatic and showed a high degree of specificity. Pyogenic cocci, clostridia, and some other bacteria were sensitive, while the coli-typhoid, haemophilic chromogenic bacilli, and others were insensitive. Pathogenic Gram-negative cocci (gonococcus, meningococcus, and *M. catarrhalis*) were sensitive, while saprophytic varieties (e.g., *M. flavus*) were insensitive, penicillin thus differing from the sulphonamides.

The action of penicillin was not interfered with by substances that inhibited sulphonamides—bacteria, bacterial extracts, pus fluids, tissue autolysates, peptones, and *p*-aminobenzoic acid. Penicillin was non-toxic to leucocytes and animals, but in low dilutions it affected the morphology of bacteria and interfered with division. As penicillin and also gramicidin were apparently of a different constitution from the sulphonamides, the isolation and synthesis of the pure active principles would open up a new chemotherapeutic field.

Trypanocidal Drugs

Prof. WARRINGTON YORKE described the action of the aromatic diamidines which were evolved by Dr. Ewins, after it had been shown that synthalin (decane diguanidine) acted on trypanosomes not by reducing the sugar but by direct toxic action. Some aromatic diamidines exhibited a remarkable trypanocidal activity. The most active were 4:4′-diamidino-stilbene, 4 : 4′ - diamidino - diphenoxy - propane, and 4 : 4′ - diamidino-diphenoxy-pentane. Cases of kala-azar had now been successfully treated by diamidino-stilbene—Indians, children in the Mediterranean area, and patients with the Sudanese variety, which was resistant to antimony. Babesia infections in dogs were cured by the stilbene and propane derivatives, the stilbene being highly active against *Trypanosoma congolense*. The compounds had a highly specific action. Drug resistance appeared to be due to a change in the surface layer of the parasite. Trypanosomes resistant to a number of compounds had now been prepared, including a diamidine preparation. It had also been possible to prepare a diamidine-resistant *Babesia* and a plasmoquine-resistant strain of *Plasmodium knowlesi* in the monkey.

Dr. F. HAWKING, discussing trypanocidal substances, said that from the phenomenon of drug-resistance four kinds of receptors on the trypanosome were recognized. Trypanocidal action comprised fixation of the drug, secondary chemical reactions inside the cell, and death. Only about the first process was much known: it occurred quickly in a few minutes and was reversible. With arsenical compounds fixation apparently depended on the tervalent arsenic atom linked to a benzene ring. Certain side chains ($-NH_2$, $-OH$) prevented fixation on animal cells but not on normal trypanosomes; the receptors of resistant trypanosomes were modified. Over a wide range the amount of drug fixed was proportional to the concentration in the surrounding fluid; in the case of acriflavine the partition ratio—concentration inside the trypanosome/concentration outside—was 8,000 for normal trypanosomes, 60 for resistant trypanosomes. Fluorescent compounds, acriflavine, and diamidino-stilbene were concentrated in the blepharoplast and cytoplasmic granules of the trypanosome.

Ehrlich's Theory

Sir HENRY DALE, after congratulating the Society on arranging a discussion meeting in wartime, emphasized the importance of having a theory of chemotherapeutic action. It was one of Paul Ehrlich's great contributions to the subject to have produced a theory which, though it would probably not survive unmodified, had given a tremendous stimulus to research. His speculations had sometimes appeared more plausible than convincing; but it was remarkable in how many cases they had eventually proved to be well founded. An example was Ehrlich's explanation of the action of certain dyes on infection by trypanosomes as due to injury of the reproductive power of the trypanosomes without affecting their other vital functions. At the time this suggestion seemed artificial and unconvincing, but when Dobell and Laidlaw found a method for growing *Entamoeba histolytica* in permanent culture *in vitro* it could be demonstrated that the action of emetine was just of this type. Another factor of chemotherapeutic activity which he believed to have importance was the "factor of persistence."

Effective chemotherapy was usually, if not always, a war of attrition rather than a "Blitzkrieg." This seemed to be the reason why a quinquivalent arsenical on the one hand, or an arseno-compound on the other, was a better chemotherapeutic agent than the arsenoxide produced by reduction from the one

or by oxidation from the other, although the arsenoxide was recognized as the directly parasiticidal agent. In the same way, sulphaguanidine seemed to owe its effectiveness in bacterial dysentery to its poor solubility, enabling it to remain in solid form in the intestinal contents and to keep up a steady, low concentration in contact with the infected mucous membrane. Aromatic diamidines, the brilliant promise of which had been made clear by the results which Prof. Yorke had reported, might similarly owe part of their superiority to their limited solubility. He ventured to suggest as problems the solution of which might greatly accelerate advance in parts of the field of chemotherapy, the discovery of a method of keeping trypanosomes alive and reproductive indefinitely in artificial culture, and the discovery of a method of treating a strain of trypanosomes which had acquired drug-resistance, so as to restore the normal susceptibility.

Some Modern Observations

Dr. D. D. Woods spoke of the interference of antibacterial agents and essential metabolites. This interference might be due to the formation of a compound between the antibacterial agent and the essential metabolite, as between mercury salts and —SH compounds, or by inhibition of an enzyme reaction involved in the synthesis or utilization of an essential metabolite. An example of this was the competitive inhibition by sulphanilamide of an enzyme reaction involved in the further utilization of *p*-aminobenzoic acid, this inhibition occurring by virtue of the chemical relationship of sulphanilamide and *p*-aminobenzoic acid. The latter had been isolated from natural sources and was a growth factor for *Clostridium acetobutylicum* and higher organisms. On this hypothesis the following substances, all chemically related to a known essential metabolite, the latter shown in parentheses, were found to have some antibacterial activity: pyridine-3-sulphonic acid and amide (nicotinic acid and amide); aminosulphonic acids (analogous aminocarboxylic acid); sulphonic acid analogue of pantothenic acid (pantothenic acid); indole-3-acrylic acid (tryptophan); barbituric acid (uracil).

Dr. H. MCILWAIN said that an organism which was deprived of the use of enzymes or metabolites by various types of interference was nutritionally more exacting than in its normal state. *Bact. coli* and *Str. haemolyticus*, inhibited by acriflavine components, required for further growth two types of material not normally required. Type I was best replaced by nucleotides: Type II by a concentrate of amino-acids, but partly by phenylalanine. In the presence of Type II compounds, but not without, artificial hydrogen carriers were further active against inhibition of *Bact. coli*. Type I compounds formed complex salts with acriflavine components. The inhibitors probably inactivated enzyme systems of which Type I compounds were essential parts, of which Type II compounds were substrates or products, and of which some could be replaced by the hydrogen carriers.

Dr. W. H. LINNELL described the relation between chemical constitution and bactericidal action in certain amino-acridines. Among the isomeric diamino-acridines, a 1-amino group caused complete loss of bactericidal activity and reduced toxicity: a 2-amino group increased activity, and this was further enhanced by another amino group in the 2-, 3-, 4- (in the other ring), or 5-positions, accompanied by increased toxicity in the case of a second 2-substituent. When two 3-amino groups (=3:7) were present activity was moderate, but the 3:8-diamino-acridine (=2:7) was as active as proflavine but less toxic. A 4-amino substituent conferred small activity, while position 5 was highly active but probably led to increased toxicity. Albert had shown that similar differences in activity existed among the five isomeric mono-amino-acridines, their activity paralleling their strength as bases and their partition coefficients between oil and water. The corresponding acridones were inactive, as were certain amino derivatives of 5:10-dihydroacridine and of iminodihydroacridine, suggesting that the intact acridine molecule was necessary.

Mr. L. G. GOODWIN said that the uncertain action of antimony in protozoal diseases, of which the resistance of Sudanese kala-azar to antimony was an example, was an added difficulty in investigating its mode of action. The active form of antimony might be the stibinoxide grouping, but while this was probable in trypanosome and schistosome infections, it was unlikely in leishmaniasis, where quinquivalent compounds were the most effective and massive dose therapy was successful.

Excretion of antimony after doses of the quinquivalent compounds or of stibophen was much more rapid than with tartar emetic. There was some indirect evidence that the rapidly excreted fraction of the drug passed through the body unchanged. Both direct toxicity action on parasites and stimulation of the host's defence mechanisms were produced by antimonials. Increased phagocytosis might be of primary importance in leishmaniasis, though histological work on the spleens of infected hamsters injected with a quinquivalent antimony compound suggested some degree of direct action.

Dr. E. CHAIN described the chemical and physical properties of penicillin in relation to its bacteriostatic action. It is a strong acid with two, or a multiple of two, acid groups. A purified barium salt gives a carbon content of 55% and an H content of 6.3%: only C, H, and O are present in the molecule. Methoxyl groups cannot be detected, but two hydroxyl groups are present. The dried Ba salt of penicillin keeps indefinitely, and in watery solution is most stable between *p*H 5 and 7. With heavy metals, except Fe $^{\cdots}$, it forms water-soluble salts. The antibacterial action is lost by oxidation with hydrogen peroxide and potassium permanganate. Dr. E. P. ABRAHAM said that the instability of penicillin necessitated three methods of purification dependent on distribution between solvents, adsorption, and reduction. The crude barium salt obtained from an amyl acetate extract of the medium has an activity of 15 to 25 units per mg. Distribution between water and ether at *p*H 2 and *p*H 6, adsorption of impurities by charcoal, and chromatographic analysis on alumina yield a light yellow barium salt with an activity of about 150 units per mg. On reduction of this material in neutral solution with aluminium-mercury couple, the remaining pigment is adsorbed by alumina. The white barium salt obtained from the supernatant has an activity of 240 units per mg. It completely inhibits staphylococcus in a dilution of 1 in 5,000,000, partially in a dilution of 1 in 16,000,000.

Dr. F. R. BRADBURY had studied the behaviour of sulphanilamide, *p*-aminobenzoic acid, and chemically related compounds, aniline and sodium benzenesulphonate, at the surface of *Bact. coli* by electrokinetic methods. The shapes of the curves relating variation of mobility with time of contact for sulphanilamide and *p*-aminobenzoic acid were quite different from those of the curves for aniline and sodium benzenesulphonate. The curves for sulphanilamide and *p*-aminobenzoic acid were similar, suggesting that the two compounds behaved in a like manner at the bacterial surface.

Prof. A. ST. G. HUGGETT said that dyes such as chlorazol sky blue F P S (Chicago blue) and chlorazol fast pink B K S were excellent anticoagulants. Structurally they resembled afridol violet, from which Bayer 205 was derived; they had a trypanocidal action, while Bayer 205 had an anticoagulant action. The dyes acted at two points in the clotting mechanism as antikinase and antithrombin. Their anti-enzyme action with blood clotting might have an analogy to their mechanism as trypanocidal agents.

PLANNING IN THE FEVER SERVICE

The Fever Hospital Medical Service Group of the Society of Medical Officers of Health met last month at B.M.A. House to consider the position of infectious diseases hospitals and of pathological services in post-war planning.

Fever Hospitals

Dr. H. STANLEY BANKS (L.C.C.), who opened the discussion, thought that fever hospitals as well as general hospitals should be regionalized. Modern fever hospital work required the equipment of a general hospital—for example, first-class laboratory service, *x*-ray department, operating theatre, and physiotherapy. Experience showed that wards for the "general sick" could quite well be a success in fever hospitals. In future fever units and general units should be combined under one administration. He pointed out that over 80% of fever hospitals, excluding those in London, had fewer than fifty beds,

and about 55% fewer than twenty beds. Many of these small hospitals should be either closed or linked up with others. It was of first importance to determine the best method of administration of a regional authority. The usual local authority method by which a chief medical officer appointed by the authority was responsible for both the management and medical direction inevitably led to a centralized bureaucracy. This might be efficient for a time by improving the backward units, but soon failed because of the atrophy produced at the periphery. Medical progress depended primarily upon the maintenance of initiative at the periphery and secondarily upon support from the centre. There should be a proper balance of power and responsibility between the two. This might be done by leaving medical direction in the hands of local and regional medical committees of senior staff. The regional committee could make itself responsible for conveying all necessary medical advice and direction to the authority, by the use of a whole-time staff if necessary. Some such scheme of decentralization of medical direction was essential to preserve the vitality of a hospital service.

Dr. L. J. M. LAURENT (L.C.C.) suggested that voluntary hospitals, owing to increasing grants from the State, were bound to come under State control. They enjoyed a semi-independence which helped medical progress but did not further mutual support. Municipal hospitals under the management of local authorities had become as efficient as voluntary hospitals, but laboured under a highly centralized administration. Any future scheme of hospital planning should avoid the disadvantages of both, and also especially avoid the perpetuation of a dual system of hospitals. The creation of a regional authority which would control both kinds, treating them as equal partners, would be a step in the right direction. A unified system of national hospitals might eventually be achieved. Modern fever hospitals approximated so much to general hospitals that they should naturally come under the same authority in any future scheme. Small fever hospitals should be replaced by larger units serving adjacent areas. As a result of the war the large fever hospitals were now treating cases of tuberculosis, chronic sick and senile patients, pneumonias, skin disorders, and casualties, besides cases of notifiable disease. After the war a diminution of infectious diseases was to be expected. The beds left vacant could no doubt be utilized for the treatment of cases similar to the above. For the needs of medical education they should be allowed to receive fever patients from larger areas than at present. The building of an infectious diseases block attached to a general hospital would be of mutual benefit to both sections.

Dr. A. A. CUNNINGHAM (L.C.C.) thought that much of the open-ward accommodation in large fever hospitals could be made available for general medical and surgical cases. This practice was initiated in London before the war. The head of a hospital should be a medical superintendent, not a layman, but there should be well-paid posts for good clinicians. Teaching hospitals should have a voice in the appointment of those who trained students in infectious diseases.

Pathological Services

Dr. J. E. MCCARTNEY (L.C.C.) said that a pathological service must provide for all classes—not only for hospitals but also for medical practitioners and public health work. It was essential to have the laboratory as near the patient as possible; therefore the technical work should be decentralized as much as possible. On the other hand, it would be advantageous to centralize and standardize, so far as practicable, supplies, equipment, conditions of service, etc. The country would be divided into a number of regions, defined geographically and according to population and existing facilities, each of which would be an administrative entity. The regions would be divided into groups each under a group pathologist, situated in the main laboratory of the group. A group laboratory would be similar to an L.C.C. group laboratory, adequately staffed and equipped. According to requirements there would be subgroup laboratories staffed by assistant pathologists, and where work was insufficient for a medical staff a technician would be employed. No separate public health laboratories as such would be provided, but the medical officer of health would be in touch with the group pathologist in his area, who would arrange for all pathological work. If epidemics occurred it would be possible to bring the laboratory to the epidemic by means of a mobile laboratory staffed by personnel from less busy parts of the region. The pathological work of the region would be co-ordinated by a regional pathologist, who should not be a whole-time administrator but attached to or in charge of a laboratory, and whose work would be mainly technical. All regions would be co-ordinated by a director of pathological services. Technical and administrative sides would be run by a committee consisting of regional pathologists and administrative staff—for example, for personnel, finance, buildings, etc. Thus the whole country would have a pathological service, co-ordinated and correlated. London would be organized on similar lines to suit its particular requirements. The L.C.C. Pathological Service now functioned as a regional laboratory service with its group and hospital laboratories, centralization of supplies, and administrative services. He suggested that this service should be the basis of a national one. As regards teaching, there should be full co-operation with University teaching departments, many of which would be the main regional laboratories.

Dr. R. CRUICKSHANK (L.C.C.) thought that the establishment of laboratory services in close association with infectious diseases hospitals needed to be greatly developed, for laboratory help was essential in the diagnosis, treatment, and control of most infectious diseases. Besides, a laboratory *in situ* helped to maintain a high standard of work in the hospital and encouraged co-ordinated investigation and research. For the proper discharge of this last function the laboratory staff must not be overburdened with routine work, and, more important, the intellectual calibre of the personnel should be high. In the past the clinical pathologist had often been regarded as inferior to his colleagues in the teaching and research departments, but with full-time adequately paid posts and encouragement of research clinical pathology should be able to attract the best brains to its service. The laboratory doing the bacteriological work of the infectious diseases hospital should also do the public health bacteriology of the surrounding area. Such an arrangement seemed specially desirable in the London area, where the liaison between the borough M.O.H. and the local isolation hospital was not as close as it might be. Field epidemiology, at present rather neglected, would also be encouraged by a system of regional laboratories such as the L.C.C. had established in London. Dr. R. A. O'BRIEN was of the opinion that no scheme for the future of the pathological services need look further than the L.C.C. group system for a plan on which to build. Dr. E. C. BENN (Seacroft Hospital, Leeds) agreed with previous speakers that hospital regionalization was inevitable. He pointed out that each part of the country had its own special problems which required individual solution, and he thought one of the major obstacles to be overcome was local prejudice. Full pathological service should be available to every hospital, but small units attached to small hospitals were as a general rule to be avoided in the interests of economy.

The Sector System as a Basis

Dr. A. G. TROUP (Willesden) endorsed the opinion that the admission of ordinary medical and surgical cases to isolation hospitals was quite a safe procedure from the cross-infection point of view, and gave his experience in this direction in the Willesden Isolation Hospital. Fever hospitals must be considered in any scheme in order that all available beds could be utilized for the maximum benefit of the community. He thought that in the London area the sector system might form the basis on which to found the post-war scheme. He supported the principle of enlarging the better and more modern fever hospitals, and either using for a different purpose or closing the others. This had been indicated in the Local Government Act of 1929 and the Public Health Act of 1936, but no progress had been made owing to the absence of compulsory powers. Finally, he supported the suggestion for some form of regional pathological service.

Dr. F. GRUNDY (M.O.H., Luton) considered that, as pathological services were so highly specialized, a regional or national organization of some sort was ideal. He preferred to substitute for Dr. McCartney's "mobility of personnel" a flexibility of personnel, as he considered that pathologists should remain

long enough in any laboratory to get well known and to gain the confidence of the local members of the medical profession. He thought that no isolation hospital should have fewer than 200 beds, in order that it might be in a position to carry at least one resident medical officer. If necessary, local government areas should be amalgamated under existing legislation, or they should be rearranged. But the future of the treatment of infectious diseases would, in his view, be found in the linkage of cubicle blocks and special wards with general hospitals, or, possibly, with children's hospitals, depending on local circumstances. Lastly he asked that planning should take into account the undoubted need for improvement in the training of nurses.

Dr. D. V. HAGUE (M.O.H., Yeovil Rural District) thought that separate infectious disease hospitals were unnecessary. Greater efficiency would be found in a fever unit of a large general hospital, as there would be greater opportunities for consultation and treatment, better education of medical students in fevers, and, in addition, all nurses would get fever and general training, which was highly desirable. Some of the present isolation hospital buildings might be used as children's hospitals, where the school medical officer might act in a clinical capacity. If regional control was adopted he agreed that the control should not be too rigid. There should be a certain amount of local autonomy and mechanism for the regular expression of opinion on local conditions to the Regional Board.

Dr. W. GUNN (L.C.C.) did not think that epidemic diseases would subside much after the war. Under a statutory organization the smaller voluntary hospitals would no longer be run as nursing homes for the benefit of the consultants. The best unit in a hospital system would be a large hospital centre with a minimum of 1,000 beds and general and special departments of all kinds. A workable scheme on these lines—the "Walton Plan"—had been worked out.

Dr. C. D. MCPHERSON (acting M.O.H., Chertsey and Walton and Weybridge Urban District) said that the lack of a pathological service was one of the chief disadvantages of a small isolation hospital. The provision of this by the E.M.S. had been of the greatest value. *X*-ray facilities were also needed, and he suggested mobile regional units. He commended a system which worked successfully in some provinces in France, where a general hospital made provision for the treatment of tuberculosis and infectious disease, and where a health department as a part of this hospital administered the other public health services.

Dr. R. W. TANNAHILL (Waltham Joint Hospital Board) said he regarded a population of 250,000 as an economic unit for providing an infectious diseases hospital in any area. Where this did not occur under one authority, a combination of districts was the solution. Such a combined authority could support a full-time resident medical officer. Some authorities were loath to close down small isolation hospitals owing to local prejudice, so that combination of districts was not always easy to obtain. The infectious diseases hospital should be able to admit all types of infectious disease occurring in the area, whether notifiable or not. This was possible only in the larger units. Many small hospitals admitted only two diseases—that is, scarlet fever and diphtheria. He saw no difficulty in the establishment of infectious wards in general hospitals. This system had been in operation in other parts of the world for many years. It was an advantage to have the services of the consultant staff and of the pathological department available for infectious cases, and the resident medical and nursing staffs could learn much from a spell of duty in the infectious wards. In the case of existing fever hospitals these could be attached to a large general hospital for the above services.

H. J. Schwartz and R. F. Maddren (*Arch. Derm. Syph.*, 1941, **43**, 374), who record two illustrative cases, state that circumscribed myxoedema is infrequent, only twenty-three cases having been recorded since it was first described in 1883 by Kocher, in two of whose patients the myxoedema was confined to the legs. The present cases were those of men aged 57 and 42 in whom the lesions consisted of plaques on the tibiae. When a biopsy specimen was taken mucinous material exuded from the wound in both cases, and microscopical examination showed the characteristic appearance of myxoedema.

Correspondence

Active and Passive Immunization against Diphtheria

SIR,—I was much interested in the two recent articles under the above heading (November 22 and 29), and particularly in the method of controlling an outbreak of diphtheria outlined in Part II. Strange as it may seem, there is at the present time no generally accepted method of controlling an outbreak of diphtheria, and existing practice varies from the enthusiast who starts by swabbing and Schick-testing everyone to the individual who believes that a clinical examination of the nose and throat is all that is necessary. Between these extremes the investigator can take his choice from quite a variety of methods, all of which seem, in practice, to give equally satisfactory results. None of these schemes can, however, be regarded with complete satisfaction. All possess obvious loopholes. The authors of the method outlined in this article are therefore to be congratulated on the completeness of their scheme. I feel, however, that there are some points which require discussion before this method of controlling outbreaks of diphtheria is generally adopted, and the following have occurred to me.

1. The number of swabs to be taken will in some cases be enormous—that is, over 600 in one of the outbreaks described. Apart from the labour involved, I wonder how many of our present laboratories could really cope with such numbers or would be able to carry out the typing and testing for virulence on the scale required. This, of course, might be used as an argument for the further extension of laboratory facilities.

2. It is obviously desirable to give the smallest dose of serum which will give a margin of safety, but is it wise to give such small doses of A.P.T.? That the authors themselves are not quite happy on this point is shown by their statement in the summary that "it might be advisable, however, in future to increase the first dosage of A.P.T. to 0.3 c.cm." I doubt whether even this dosage is adequate for the younger children. Certainly many experienced immunologists favour higher doses.

3. The authors state that "all carriers were isolated or segregated as soon as the results of swabs were known." But they do not say how this was accomplished. In a day school there are three alternatives: isolation in the home; segregation in the school combined with home isolation; and admission to an infectious disease hospital. The first two are likely to be very unsatisfactory for many obvious reasons. To suggest home isolation of the healthy child for a period up to six weeks is, in the vast majority of instances, to ask the impossible, and segregation at the school would be difficult and unfair to the child; also to send the carrier home has the double disadvantage of transferring the child from a substantially protected community to one not so fortunately placed, and of removing the child from school supervision. Admission to an infectious disease hospital would be contrary to modern practice, and in most cases impracticable owing to lack of available bed accommodation—for example, twenty-seven carriers were found in one of the outbreaks reported.

The plain truth is that there is no satisfactory way of dealing with a healthy carrier of diphtheria, and one wonders whether it is really worth while going to the great deal of trouble and expense of finding them, except, perhaps, as a matter of academic interest. In addition, it is a debatable point whether healthy carriers do not, in fact, do more good than harm to the comunity. How else, in the absence of immunization, is the child to gain any immunity at all? Of course it is both safer and surer to gain one's immunity by artificial means, but I look forward to the day when this view is universally acknowledged and acted upon, but until immunization is far more widely accepted than at present very many children will have to gain their own natural immunity by subminimal doses of diphtheria bacilli picked up from time to time from healthy carriers. For instance, the authors Schick-tested some 300 youths between the ages of 14 and 24 at Turner's Court Training Colony and found that only 36% gave positive reactions. This implies that 64%, or approximately 192 youths, had previously attained a satisfactory level of immunity, some possibly by artificial immunization, but many must have gained their immunity naturally—

that is, by close contact from time to time with carriers of diphtheria bacilli.

I feel, therefore, that although the method outlined by the authors is sound in theory, my own preference would be to omit all swabbing and Schick-testing and rely on combined active and passive immunization given in adequate dosage and followed by clinical supervision throughout the period of relative susceptibility—that is, from three to six weeks after the first inoculation.

A further suggestion has occurred to me which, if practicable, would eliminate all risk of cases arising during this period of relative susceptibility, and that is that the second dose of A.P.T. should be given after an interval of three weeks and should be accompanied by a second dose of serum. As to whether this is feasible or not I am not qualified to judge, as it will depend on how far the refined serum of to-day has eliminated the bogy of anaphylaxis. I should be very interested to hear other views on this point.—I am, etc.,

Birmingham, Dec. 12. J. F. WARIN, M.D., D.P.H.

Control of Diphtheria in Schools

SIR,—In your issue of November 29 (p. 759) my colleagues and I described a method for the immediate control of diphtheria outbreaks by making use of combined active and passive immunization together with segregation of carriers for six weeks. Dr. William Gunn and Dr. Robert Cruickshank of the North-Western Fever Hospital (December 13, p. 861) criticize this method on the grounds that preliminary Schick-testing should be the rule; that combined active and passive immunization should be given only to the positive reactors; that the detection of carriers is beyond the capacity of most laboratories in this country; that there is insufficient accommodation for the segregation of carriers in isolation hospitals; that there is no power to remove carriers to an isolation hospital; and that, in any case, carriers may be beneficial by serving to maintain an adequate general level of immunity in the population. These criticisms strike at the root of the method we advocate, and cannot be left unanswered.

In our opinion preliminary Schick-testing is waste of time, since it allows the epidemic to progress unchecked for another one, two, or three days. The administration of serum to all those exposed to risk four to six hours after Schick-testing may get over this objection; but, except in a residential institution, it presents too many difficulties to be practicable. Schick-testing calls for more injections and an extra visit of the laboratory staff. The only benefit that Dr. Gunn and Dr. Cruickshank themselves claim for it is that it avoids the necessity of injecting Schick-negative pseudo-reactors with prophylactic toxoid. In view of the desirability of stopping a diphtheria outbreak at once, such a consideration seems to be of minor import; moreover, the unduly severe reactions that may follow the injection of toxoid into these persons can be largely avoided by using T.A.F. for subjects over 14 or 16 years of age. The restriction of active immunization to Schick-positive reactors overlooks the possibility of diphtheria developing in negative reactors, as occurred in a recent outbreak in which preliminary Schick-testing was used. The practice of giving combined active and passive immunization without the simultaneous removal of carriers is open to two objections: first, it depends for its success on obtaining consent for immunization from the parents of all the children; secondly, it neglects what we have referred to, for want of a better term, as the "intermediate phase of relative susceptibility" between the wearing off of passive and the development of active immunity, during which, in the presence of virulent carriers, a proportion of the inoculated children are liable to develop diphtheria. That this is no mere theoretical danger is shown by the experience of Gierthmühlen and Voges at Hamburg, described in our article.

In mentioning the difficulty of examining swabs from 200 to 300 children on tellurite blood agar plates Dr. Gunn and Dr. Cruickshank were presumably referring to the Provinces, and not to London, where the examination of swabs from a few hundred children ought to be well within the capacity of the L.C.C. pathological service. So far as the Provinces are concerned, such a task may have been difficult for many laboratories before the war, but with the establishment by the Medical Research Council of a chain of Emergency Public Health Laboratories throughout England and Wales, which can draw for help on the three central laboratories at Oxford, Cambridge, and Cardiff, this objection now loses much of its force. Incidentally, all these laboratories are prepared to undertake field work, so that not only the examination of the swabs but often the swabbing itself could be arranged for satisfactorily. Isolation hospitals may be short of beds, and there may be no power to remove carriers to them; but carriers can be kept at home provided the other members of the household are immunized, and there *is* power to exclude carriers from school.

As regards the final contention that carriers may be a benefit to the community, this is on a par with the argument that raw milk is preferable to pasteurized because, by virtue of the tubercle bacilli it not infrequently contains, it helps to immunize children against pulmonary tuberculosis in later life. Even if it did do so, which is doubtful, it is a wasteful method, involving as it does the death of about 1,500 to 2,000 persons annually from tuberculosis of bovine origin. Surely, in a disease like diphtheria, where we have a method of prophylaxis of proved value, is not the scientific procedure to immunize the population and keep them immunized rather than to trust to the haphazard and uncontrollable method of latent immunization through infection from carriers?—I am, etc.,

Oxford, Dec. 13. G. S. WILSON.

Medical Psychology

SIR,—Reading such letters as that by Dr. F. M. R. Walshe (December 13, p. 858) one is astounded at the support unconsciously given by the writer to the arguments of medical psychologists. Was ever such prejudice displayed? Had Dr. Walshe taken the trouble to look into the past work of those he so seriously attacks he would find a most distinguished record of careful research, published in reputable journals, with adequate controls, and otherwise conforming most rigidly to the very best principles of scientific research to the credit of at least one of the authors of the article he criticizes. Dr. Walshe is quite ignorant, it would seem, of the great body of work done by such distinguished men as Prof. Millais Culpin and others upon "normal" and "abnormal" groups from the population. For example, Dr. Culpin took a group of Post Office workers and compared them with a random sample of the populace. After a lapse of years he again examined his Post Office group, and found that his predictions as to their psychological history had been fulfilled to a remarkable degree.

Many other medical psychologists have examined such groups and "normal" control groups, so that the percentage of psychological anomalies to be found in a so-called normal sample of the populace is well known. Wittkower and A. T. M. Wilson, when examining the personalities of patients with peptic ulcers, compared this group, I believe, with a group of patients admitted for the treatment of hernia. Such groups have been selected by other doctors, mingled, and presented to medical psychologists for examination. They were able with a reasonable degree of accuracy to separate the two groups.

Dr. Walshe, in common with other critics, will not permit himself to regard the psychologist as he would regard any other scientific investigator—namely, as one seeking to discover the truth whatever it may be. If he is really interested in this subject of so-called psychosomatic disorder, I recommend him to refer to Flanders Dunbar's book, in which all the work done throughout the world over a considerable number of recent years is summarized and reviewed with full references.—I am, etc.,

Dec. 13. GEORGE PEGGE.

Publicity for Preventive Medicine

SIR,—It will interest your correspondent Surgeon Lieut. W. B. Jamison (December 13, p. 860), to know that in 1936 the British Empire Cancer Campaign began to organize lectures to the laity on the subject of cancer. This was started in a small way in three counties, and was judged by the "fan mail" to be so successful that it was greatly extended throughout the country, six counties being organized each year. All activity ceased on the outbreak of war. During these years 1,256 lectures were given to audiences totalling over 57,000 people, for the most part by local medical men after careful consultation with headquarters. At many such lectures a

specially prepared cinema film called "Out of the Shadow" was shown.

I agree with Dr. Jamison that much could be done by talks on the wireless, but such talks could not altogether replace the more intimate lecture to a small audience which is followed by questions and answers. It is to be hoped that under the Cancer Act the education of the public concerning cancer by means of such lectures will be carried out on a much larger scale, as in my opinion this is the only way to get rid of the fear which is one of the main obstacles preventing the early diagnosis of the disease.—I am, etc.,

MALCOLM DONALDSON,

London, W.1, Dec. 15. Chairman of the B.E.C.C. Propaganda Committee.

Haemoglobin of Pregnant Women

SIR,—During the years 1937 and 1938 and the first two months of 1939 the haemoglobin of patients on their first attendance at the ante-natal clinic of an L.C.C. hospital in North London was determined by Haldane's method. These tests were done at first by Dr. S. H. G. Robinson and later by Dr. W. W. Kay, who has made an extensive analysis of the results which, it is hoped, will be prepared for publication later. There were 2,005 patients, the average of the figures representing the percentage haemoglobin was 84.7, and 107 patients (5.3% of the total) had less than 70% of normal haemoglobin.

After the beginning of the war determinations of haemoglobin were not made for each ante-natal patient until early in 1941. Drs. H. A. Ash and J. M. Alston have supervised from the middle of April to the middle of December of this year the testing of 814 patients at the time of their first attendance, and the average of the haemoglobin figures was 70.8, which is 13.9 less than the comparative figure for the group before war began, and 319 of these (39%) had less than 70% of normal haemoglobin.

In suggesting that it may be concluded that pregnant women in this part of London are distinctly more deficient in haemoglobin than before the war we draw attention to a number of factors which show, we think, that the two groups of figures are comparable. First, the test was made from freely flowing capillary blood in the pre-war group and in almost 40% of the wartime group; from the remainder of this second group venous blood kept fluid by shaking with crystals of ammonium and potassium oxalate was used; the average percentage figure for the specimens taken from venous blood was 2.5 less than for capillary blood and 1.5 less than for the whole of the wartime series. Secondly, before the war many different standard haemoglobin tubes were used for the series of determinations, and these tubes were, by general experience of them, believed to be satisfactory, but since war began it has been found by many pathologists that newly supplied tubes are often inaccurate. For that reason, by the kind collaboration of Dr. Lucy Wills, Royal Free Hospital, the tube used for the determinations in this year's series was checked with and found equal to a standard authenticated by oxygen-combining power. Thirdly, grouping of the patients by ages showed a distribution which was nearly the same before and since the war, and at any rate it was found in the pre-war series that it was only after the age of 35 years that age alone appeared to be associated with haemoglobin significantly below the average. In the pre-war series 8% of the patients were over 35 years and in the war series 9%. Fourthly, the almoner of the hospital has told me that, although she is unable to make an exact comparison of economic circumstances of the patients in the two groups, she does not think that since the war there have been less favourable financial circumstances than before. Fifthly, the distribution according to stage of pregnancy was sufficiently similar in the two groups.

The average figure for the haemoglobin of patients in 1937 was almost the same as 1937 and 1938 taken together (83.5% and 84.7% respectively), so that the state of haemoglobin deficiency was apparently stable in 1937 and 1938. The decrease found in 1941, therefore, is not the continuation of a progressive decrease which was going on before the war. In 1937 and 1938 anaemia was present, as shown by the average haemoglobin value of 84.7% and by the fact that almost exactly two-thirds of the patients for whom the red corpuscles were counted had a colour index below 0.94. An analysis of colour indices has not been made in 1941, but from the fall of the average haemoglobin value to 70.8% the anaemia is obviously intensified. The conclusion which we think may be drawn is that during this year food taken by pregnant women in this part of London has been inadequate in iron.

We thank the medical officers and members of the nursing staff of the hospital for assistance; and for care and enthusiasm in technical work during this year we are indebted to Mr. R. Rodnight.—We are, etc.,

W. W. KAY, M.Sc., M.B.
J. M. ALSTON, M.B., M.R.C.P.Ed.

Group Laboratory, Archway Hospital, N.19, Dec. 12.

Haemoglobinometry

SIR,—In their letters Dr. Robert Campbell (November 22, p. 747) and Dr. A. J. E. Mills (December 6, p. 823) point out difficulties in determining the amount of haemoglobin present in blood. It needs to be emphasized that the usual manner of expressing the haemoglobin value is as a percentage of an arbitrary normal, which *varies* according to the method employed. The normal value is accepted as 100%, this being convenient for calculating the colour index. In Haldane's method this 100% is equivalent to 13.8 grammes haemoglobin per 100 ml. blood; whereas on the Sahli scale the 100% represents 17.3 grammes haemoglobin, or 124% Haldane.

When employing either method these differences must be taken into account, and each tube used for the dilution of the blood should be carefully examined before use. Most haemoglobin tubes are graduated as grammes Hb%, and also according to the arbitrary percentage of Sahli or Haldane. If these tubes are interchanged it is evident that anxiety as to the accuracy of haemoglobin determinations may arise. It would therefore seem desirable that haemoglobin estimations should be reported on a scientific basis as grammes Hb/100 ml. rather than a percentage of an alleged normal. If the latter be used then the method employed must be stated.

Regarding the use of the Sahli instrument, a wait of ten minutes before matching the colour developed with the standard suffices for clinical use. It may be remarked that provided the same technique is employed each time comparable values will be obtained as to the progress of any case.—I am, etc.,

Miller General Hospital, S.E.10, Dec. 9. W. SMITH.

Red-cell Suspensions in Anaemia

SIR,—I was interested to read Dr. K. B. Rogers's letter on the above subject (December 6, p. 823).

I have given about forty transfusions of cell concentrate, but I find it very difficult to fix with any precision the haemoglobin rise per volume of concentrate given. This must depend on so many factors, such as blood volume, body weight, and capacity of storage of transfused cells, that even an approximation cannot be reached which will be applicable to all cases.

Perhaps an example of two recent cases will emphasize this. These patients were transfused with blood drawn off on the same day, stored for the same time (two days), and decanted on the same day. Further, the same volume was used, and other factors were strictly comparable. The first case, a thrombocytopenic purpura, had a rise of 1% haemoglobin per 28 c.cm., while the other, a gastro-enterostomy, had a rise of 1% per 35 c.cm. The variation in results will be found with fresh blood transfusion also.

It seems to me that it is impossible to achieve mathematical precision in a matter with so many variables.—I am, etc.,

ARCHD. L. GOODALL, M.B., Ch.B.,

University of Glasgow, Dec. 15. F.R.F.P.S., D.P.H.

Congenital Arteriovenous Anastomosis

SIR,—The interesting case described by Dr. A. G. Watkins (December 13, p. 849)—whether there is a free arteriovenous communicatioin or not—shows some dilatation of the internal saphenous vein and increased length of long bones in the affected leg, and therefore obviously belongs to the somewhat loose group which in 1918 (*Brit. J. Child. Dis.*, **15**, 13) I described under the heading "Haemangiectatic Hypertrophy of Limbs," including congenital phlebarteriectasis and so-called "congenital varicose veins." On these last I wrote a further note in 1936 (*Brit. J. Child. Dis.*, **33**, 102). Since 1918 a considerable number

of cases have been described in England and abroad as examples of "haemangiectatic hypertrophy." The increase of length probably occurs only when there is increased blood supply to the growing skeleton of the limb, and is occasionally imitated in Nature's experimental laboratory when a child's long bone is subjected to chronic active hyperaemia as the result of congenital syphilitic osteitis or some other chronic bone infection. Though continual active hyperaemia is the probable direct exciting cause of the increased length of bones in haemangiectatic hypertrophy, the cause of the congenital (developmental) abnormality in the blood vessels remains almost as unexplained as does the monstrous growth of fingers or toes affected by genuine gigantism.

The occurrence of the temporary discharge of lymph suggests that in addition to the haemangiectatic there is also a lymphangiectatic condition present, and that the limb is destined to become the site of intermittent lymphorrhagia. Wherever there is developmental lymphangiectasis a leakage may occur, which, according to the site, will be manifested by lymphorrhagia on the surface of the body, chylothorax, chylous ascites, chyluria, or chylous discharge from the uterus or elsewhere; the discharge of lymph or chyle in such cases may be only temporary or intermittent.—I am, etc.,

London, W., Dec. 13. F. PARKES WEBER.

Encopresis in Children

SIR,—I was interested in Dr. Charles Burns's article on encopresis in children (November 29, p. 767).

I am not competent to discuss the psychological aspect of the matter, but would like to point out that there are children who exhibit encopresis because of faecal impaction of the rectum, a condition brought on by long-standing failure to empty the lower bowel satisfactorily. This is comparable to overflow incontinence of the bladder, and can be easily detected by rectal examination. I had several such cases, and found that the only satisfactory method of treatment, and one usually affording permanent relief, is digital removal of the faeces from the rectum.—I am, etc.,

Selly Oak Hospital, Birmingham, Dec. 10. A. M. NUSSEY.

Combined Intra-uterine and Extra-uterine Pregnancy

SIR,—Dr. R. B. Leech's interesting case reported in the *Journal* of December 6 (p. 805) reminds me of a case which came under my care while I was on the staff of a mission hospital in Northern Nigeria. My case, although not going on to term like Dr. Leech's, is nevertheless unusual enough, I think, to record.

In October, 1939, I was suddenly called to see a young Fulani woman of about 25 years of age who had been staying on the hospital compound looking after her son, who was receiving treatment for sleeping sickness. She had complained of sudden abdominal pain and then collapsed. On examination the abdomen was extremely tender and showed evidence of free fluid in the peritoneal cavity. There was a history of three months' amenorrhoea, and a diagnosis of ruptured ectopic gestation was made. At operation the peritoneal cavity contained free blood, the sac, situated in the right tube, having ruptured directly into the peritoneal cavity. The condition was dealt with along the usual lines. While performing the operation I particularly noticed that the uterus was enlarged considerably more even than one would expect for a three-months pregnancy. All went well until the third day after the operation, when the woman complained of "labour-like" pains, and later in the day miscarried and produced twin males, each foetus being well formed and about the size of a three-months pregnancy. This was the patient's third pregnancy, and she afterwards made an uninterrupted recovery.

A case of triple pregnancy, one of which was extra-uterine and the other two intra-uterine, must surely be a rarity.—I am, etc.,

Pulham Market, Norfolk, Dec. 9. C. E. LANGLEY.

Nail Lacquer Dermatitis

SIR,—Your annotator (December 13, p. 855) states that "little has been heard in this country of dermatitis due to cosmetic preparations for the nails." During the past few weeks I have seen two cases in which sudden outbreaks of swelling and dermatitis of the eyelids, face, and neck have been associated with a sensitivity to a certain brand of nail polish. Positive patch tests have been obtained, and it is hoped to obtain from the manufacturers samples of the constituents in order to determine the nature of the causative factor.

One lady had been resident in the country for many months. Having children to attend and housework to do she had not used nail polish except on two separate occasions many weeks apart, when the nails were lacquered the night before a proposed trip to London. On each occasion the patient wakened next morning with an intense rash over the eyelids, face, and neck, and herself volunteered the information that she thought the rash associated with the nail-lacquering technique. There was no rash on the hands.

If the co-operation of the manufacturers can be obtained I hope to make a further communication on this subject at a later date.—I am, etc.,

London, W.1, Dec. 13. GEORGE BRAY.

Rehabilitation of the Injured

SIR,—All interested in the problems of the physically disabled must welcome the schemes initiated by the Ministry of Health and the Ministry of Labour and National Service which are referred to in your leading article of December 6 (p. 812). In doing so, however, it is important to remember that we are still far from a "comprehensive national scheme of rehabilitation."

While the Ministry of Labour's plans for the training and resettlement of the disabled will, or can be made to, apply to all classes of disabled, the rehabilitation schemes inaugurated by the Ministry of Health are at present much narrower in their application. They exclude large sections of the accident-disabled—sufferers from traffic accidents, to mention only one—the disease-crippled (unless associated with war service), and children. For all these people it has become more, not less, difficult to obtain specialized treatment, owing to the wartime limitations on normal hospital services.

Those whose work brings them much into contact with the permanently disabled know what a high proportion might have been cured by treatment at an earlier stage and could still be greatly benefited given facilities which, for them, are not available—tragic evidence of the inadequacy of the orthopaedic services which existed before the war, even for children, and of the distance which must still be travelled before anything like a complete national rehabilitation service is achieved. I suggest that it never can be until the many aspects of this complex problem cease to be dealt with piecemeal by a number of different Departments and are instead co-ordinated under a single authority—a Rehabilitation Board—whose sole criterion would be the fact of disablement rather than its cause or the disabled's category.

Glad as we must be of the present advance, so long overdue, the ultimate objective should not be lost sight of. The nation cannot afford to waste its assets, least of all its man-power. What can be done to avoid this by treatment has long been demonstrated. How far training can be effective is becoming increasingly realized. For the past sixteen months men with a high degree of disablement have been training under the munitions training scheme of the Ministry of Labour, and are proving their capacity to work on equal terms with the able-bodied, even under the exacting conditions prevailing in wartime industry.—I am, etc.,

Exeter, Dec. 10. GEORGIANA BULLER.

Medical Man-power

SIR,—As one of the witnesses before the commission investigating medical man-power, I am able to throw some light on certain points raised in Mr. H. J. McCurrich's letter (December 6, p. 826). The witnesses with whom I was associated had all been released from the Services to attend to urgent and essential duties among the civil population. They were thus able to give their evidence freely and, I think, fairly.

Where detachments of separate Services are stationed in close proximity it should obviously be possible for one medical officer to care for the medical needs of soldier, sailor, or airman, providing authority for this step could be obtained from the Departments concerned.

I am entirely in agreement with Mr. McCurrich in his view that sanitary N.C.O.s could take over the greater part of the routine inspections in camps. In actual fact this progressive step had already been taken by the D.A.D.H. (M.O.H.) in the area where I was stationed. He usually sent his sanitary

sergeant to make a periodic inspection of barracks, and any further action depended on his report. O.C.s of regiments are extremely keen keeping sanitation up to a high standard, and it was rare to find any serious fault.

In recruiting depots where there are a large number of inoculations there seems no reason why trained nurses, male or female, should not be used under the supervision of a M.O. His suggestion that the office of D.A.D.M.S. should be taken over by lay personnel is a more revolutionary one and not likely to commend itself to the powers that be, but it is undoubtedly feasible. A D.A.D.M.S. is the personal private secretary of the A.D.M.S., and it has always seemed a great waste of a healthy young doctor to make him sit on an office stool wading through indents and answering questions which his chief clerk could do equally well. If it is not possible to introduce laymen or women there is no doubt that women doctors could adequately fill this post in suitable areas.

Junior medical officers in field ambulances might be replaced by officers trained in hygiene and in the treatment of casualties during evacuation to hospital. So much of the work of a field ambulance is similar to that of a routine duty of any company officer, and again it seems a pity that a skilled tradesman should be used for this purpose.

Lest it should be thought that this letter is directed entirely against extravagance in medical man-power in the Forces, it is only fair to say that in the larger cities, if the three main services—namely, public health, hospitals, and general practitioners—pooled their resources there could be a considerable saving of medical man-power, and, what is equally important, the public would not suffer.—I am, etc.,

Birmingham, Dec. 9. R. C. L'E. BURGES.

The Nation's Teeth

SIR,—Referring to Captain G. E. King-Turner's letter on "The Nation's Dental Services" (December 6, p. 827), I beg to point out that, during this war crisis, an exceptional opportunity presents itself for a National Dental Survey which would confirm and accentuate the views expressed in that letter. There is something radically wrong with the nation's dental services; they are not getting positive results. As factory medical officer to the Ministry of Supply, with over twenty-five years' experience of physical examinations in H.M. Navy, I now examine weekly some 300 to 400 new entries of both sexes, drawn from every section of the community. While taking stock of the teeth in a general way, I have also found time to keep records of between five and six hundred—a comparatively small number to date owing to other duties. But from this summary survey one fact emerges clearly—namely, that, despite the treasure that is being expended yearly on school dental services and on dental research, the standard of the nation's teeth has depreciated considerably during the last twenty-five years.

Among the thousands examined here, five Asiatics presented themselves—four Indians and one Burmese. One of these men had had three teeth missing, the other 29 being perfect and free from blemish, and of the three extracted, one sound tooth had been extracted in error. The contrast between the Asiatic dental standard and our own might be described briefly as follows: The teeth were larger and stronger, apparently more fully developed; the arches were wide, making room for full development; uniformity and white ivory aroused one's wonder and envy. All the surgery staff were invited to inspect and admire the beauty of all five as a contrast to what we have become accustomed to.

In examinations of over 1,000 Indian and 1,000 Chinese labour recruits on the Singapore Base (1923 onwards) 87% of Indians and 67% of Chinese exhibited this standard of complete and perfect teeth, free from defect, every tooth doing its duty. A similar examination of the active service personnel of one of H.M. ships in 1921, representing a highly select and well-cared-for part of the general population, revealed only 2.75% of the standard of perfection, but even these lacked the uniformity and ivory-like whiteness of the Asiatic teeth.

I suggest that the opportunity is at hand, and that a National Dental Survey is one of the urgent needs of the moment in the interests of the nation's health.—I am, etc.,

Dec. 6. D. H. C. GIVEN, M.D., D.P.H., Surgeon Captain, R.N. (ret.).

Obituary

G. DE BEC TURTLE, M.D., M.R.C.P.

The passing of Godfrey de Bec Turtle removes another well-known medical man from the West End of London. Dr. Turtle was a man of many activities: at the time of his death on December 4 he was president of the Medical Defence Union, the Medical Sickness Assurance Society, and of the Clinical Section of the Royal Society of Medicine. He was also medical superintendent of the Luton and Dunstable Hospital, and it was in this hospital that he died after a very short illness.

He was an energetic and enthusiastic worker, and one who always believed in doing things in the right way no matter how much trouble it caused him. After an early medical education in Durham and King's College Hospital he held several house appointments, and became obstetric registrar and tutor to King's College Hospital. He practised for many years in the Hyde Park area, and was constantly to be seen exercising in the Park before breakfast; he always maintained that riding was the best exercise for a busy man, and he advised it for many of his patients.

It is impossible to cover all Turtle's activities, for they were legion. He was interested in the Post Office in the Paddington district, and was one of their district medical officers. He was an ardent supporter and a past president and treasurer of the Harveian Society of London, and the success of that society and its popularity are in great part due to his influence. He also found time to devote two mornings a week to the Public Dispensary, Drury Lane. He was consulting physician to Brentwood Hospital and to the Margaret Street Hospital for Consumption. He devoted much time and energy to the Royal Society of Medicine and was a most useful councillor, having filled the post of treasurer with distinction. Turtle was at his best at one of the social functions of the society, and was always keen to further the society's interest.

He leaves a widow, a son who is in the Royal Navy, and two daughters who are doing war work.

Medical missionary work in China has suffered a severe loss in the death of Dr. FRANCIS HENRY (ROBIN) MOSSE. The son of the Rev. E. H. Mosse, vicar of St. Paul's, Covent Garden, Dr. Mosse was educated at King's School, Canterbury, and Trinity College, Oxford. He studied medicine at King's College Hospital, and in 1913 qualified M.R.C.S., L.R.C.P.Lond. During the last war he served as temporary captain in the R.A.M.C. in Egypt and Palestine, and was with General Allenby's forces at the capture of Jerusalem. But Dr. Mosse's heart was set on medical missionary work, and in 1920, after taking the M.R.C.P., he sailed for China, under the S.P.G., to take up the post of physician to the Cheloo Christian University, Shantung, North China. There for twenty years Robin Mosse trained young Chinese men and women. "A picked group of the finest students in the world," he called them, and he counted himself "the happiest man in Asia" in being allowed to serve them in the name of Christ. He worked with them in refugee camps, in times of flood and famine, as well as in the lecture halls and wards of Cheloo Hospital. After the Japanese occupation of North China the majority of the 4,000 students at Cheloo trekked west to free China, but the hospital remained and Dr. Mosse stayed with it. Early this year he fell ill with tuberculous trouble, and was sent to the U.S.A. for treatment. He seemed to be making good progress, and his death, which followed an operation, was sudden and unexpected.

The death is announced of Dr. HENRY KING DAWSON, senior practitioner in the Ashtead area of Surrey. He was educated for the medical profession at Newcastle-upon-Tyne, and graduated M.B., B.S. of Durham University in 1892, proceeding to the M.D. in 1896. During the South African War he served as a civil surgeon with the Gloucestershire Yeomanry, and later with the 9th Lancers and the Coldstream Guards. He began practice at Ashtead in 1902. On the formation of the

Territorial Force Dr. Dawson received a commission in the R.A.M.C.(T.), and on the outbreak of war in 1914 was embodied for service and joined the 6th London Field Ambulance, of which he was later given command with the rank of lieutenant-colonel. For his services in France he was thrice mentioned in dispatches and awarded the D.S.O. Returning to practice at Ashtead he took part in many local activities, and during the present war was appointed medical officer in charge of the local mobile unit. He was on terms of friendship with all his colleagues, and until the passing of the National Insurance Act had been a staunch member of the B.M.A.

The Services

HONORARY PHYSICIAN TO THE KING

Colonel R. Sweet, D.S.O., I.M.S., has been appointed Honorary Physician to the King in succession to Major-General (local Lieut.-General) W. H. Hamilton, C.B., C.I.E., C.B.E., D.S.O., late I.M.S., who has retired.

ARMY AWARD

The Commander-in-Chief, Middle East, General Sir Claude Auchinleck, has, by the authority of the King, approved the immediate award of the Military Cross to Captain John Bissill Heycock, R.A.M.C., for gallantry in action during recent operations in the Western Desert.

CASUALTIES IN THE MEDICAL SERVICES

INDIAN MEDICAL SERVICE

In an India Office Casualty List published on December 11 Colonel EDWARD GALWEY KENNEDY, I.M.S., is recorded as having died. He was educated at Queen's College, Cork, and graduated M.B., B.Ch., B.A.O., of the Royal University of Ireland in 1909. In the following year he entered the I.M.S. as lieutenant, became captain in 1913, major in 1922, and lieutenant-colonel in 1930. In 1937 he was promoted to colonel, and in the same year was appointed Deputy Director-General of the I.M.S. He had been a member of the British Medical Association since 1915.

Captain S. S. Apte and Captain Bazley Rabbi are included as "Died" in an India Office Casualty List published on December 11.

INDIAN MEDICAL DEPARTMENT

Captain R. H. F. Parkinson, D.C.M., is included as "Died" in an India Office Casualty List published on December 11.

Wounded

Assistant Surgeon K. C. Clarke.

Universities and Colleges

UNIVERSITY OF CAMBRIDGE

At a Congregation on December 6 the following medical and surgical degrees were conferred by proxy:

M.D.—T. D. Day.

M.B., B.CHIR.—R. E. M. Pilcher, R. E. W. B. Comerford.

UNIVERSITY OF EDINBURGH

At a graduation ceremonial on December 12 the following degrees and diplomas were conferred:

M.D.—Fanny B. Chisholm (*née* Mackintosh), C. A. Gleadhill, *A. M. Macdonald, Lieutenant, R.A.M.C., †J. H. Patterson, Captain, R.A.M.C., †A. J. Rhodes.

M.B., CH.B.—I. R. W. Alexander, R. F. Antonio, B. A. Bembridge, G. D. Bonner, W. Boyd, A. K. Brown, L. F. Brown, W. J. J. Bryden, Rosemary E. Buchan, W. Campbell, J. M'D. Corston, J. Devine, N. G. Douglas, N. K. Farley, W. D. Frew, E. R. L. Gregson, C. J. C. Hinnrichs, Jean Leith, Anne W. Maclennan, D. Malcolm, A. M. Plant, D. Pottinger, S. I. Pugh, †Anne R. M'C. Ross (*née* Sellar), Margaret C. Tate, H. D. Thompson, D. R. Tipping, †F. Viedge, A. L. Wallis, J. A. Watt, D. B. Wiseman.

DIPLOMA IN PUBLIC HEALTH.—†A. S. Qunta, T. M. Small, †Helena S. L. Taylor (*née* Lauder-Thomson).

DIPLOMA IN MEDICAL RADIOLOGY.—R. A. M'Kail.

D.Sc.—In the Department of Pure Science: †C. E. van Rooyen, M.D., Major, R.A.M.C.

* Awarded gold medal for thesis. † *In absentia.*

POLISH SCHOOL OF MEDICINE IN EDINBURGH

M.B., CH.B.—W. K. Gatuszka, Jadwiga Mickiewicz, S. Schta, F. Solich.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At an ordinary meeting of the Council of the Royal College of Surgeons of England, held on December 11, with Sir Alfred Webb-Johnson, President, in the chair, Mr. Seymour Barling was reappointed representative of the College on the Court of Governors of Birmingham University, and Mr. L. E. C. Norbury was reappointed representative on the Central Council for District Nursing in London.

A Final Examination for the Fellowship will begin on Thursday, February 5, 1942.

Diplomas

Diplomas of Fellowship were granted to the following candidates:

E. O. Harris, H. E. Blake, P. M. G. Russell, V. A. J. Swain, T. L. S. Baynes, B. G. A. Lilwall, E. W. O. Adkins, G. A. Fairlie-Clarke, A. R. Leask, S. I. Green, H. J. Richards, J. Moroney, G. M. Müller, A. G. Apley, J. B. Kinmonth, D. A. J. Ebrill, H. E. Hobbs, W. H. Weston, E. E. T. Taylor, L. H. Aitken, H. B. Boctor, C. H. Cullen, S. Eisenhammer, J. D. Gray, C. G. D. Halstead, J. N. Nish, C. M. Ley, W. Parke, J. J. Richmond, W. E. Springford, N. Waddle.

Diplomas in Anaesthetics were granted, jointly with the Royal College of Physicians of London, to the following candidates:

J. B. Adams, J. H. Crawford, H. de L. N. Davis, D. C. Devitt, R. R. Dickson, J. K. A. Dorman, H. Edwards, H. R. W. Franklin, Ysobel M. Garland, E. F. Gleadow, T. C. Gray, P. S. A. Heyworth, W. Kupfermann, C. B. Lewis, A. M. McKinlay, J. V. Mitchell, L. G. Morrison, G. B. Oliver, J. Patterson, G. Quayle, G. M. Rose, Enid B. Roulston, R. D. Scott, R. P. W. Shackleton, A. A. Shein, Janet Todd, E. C. Whitehall-Cooke, Joyce Worthington, A. M. Young.

Medical Notes in Parliament

National Service Bill

On the second reading of the National Service Bill it was stated for the Government that one woman doctor would be present at the medical examination of women. It was also stated that no woman would be taken from, among other services, full-time Civil Defence work, nursing, and domestic work in hospitals, and teachers would not be disturbed.

During discussion on December 10, in Committee on the National Service Bill, of an amendment proposing not to compel women to undertake service with the Armed Forces, Mr. HENDERSON STEWART said the conditions in A.T.S. camps were bad and also the physical conditions of the girls in many cases. Mr. BEVIN replied that the physical conditions were capable of improvement. With the Service Ministers he was trying to arrive at a proper standard such as they had on the munitions side. The Cabinet agreed that as Minister of Labour he should create hostels near the camps. His Department had received allegations concerning one camp, but an independent investigation showed there was not a single case of venereal disease there. The proposed amendment was negatived.

Subsequently Major HADEN GUEST asked what provision Mr. Bevin would make for detailed hygienic and medical supervision in the new factories which he was providing. No machinery existed, and there was a shortage of medical manpower. Mr. MARTIN asked what measures the Minister intended to take to look after the health of the people who were called up. If women who were constripted became unfit, could they leave their employment on a medical certificate of their own doctor, or would they have to get a certificate from some medical board? Mr. BEVIN said that he could not deal with the nationalization of the medical services under this Bill. The Services were being constantly expanded on the health side, and he had made provision for compulsory medical service in industry. That innovation had expanded and now included nursing.

The clause imposing compulsory service for women was carried by 223 to 0.

The debate was resumed on December 11. On the clause extending the age of men's military service to 50 Mr. MAXTON moved to reduce the upper age to 45. He said there would be a higher rate of sickness, of breakdown, and of discharge in these grades, and either a huge bill to pay through the Ministry of Pensions or a widespread grievance through the country if these men were told their illnesses were those they might have got in civil life and were not attributable to or aggravated by war service. Sir WALTER GREGG said the Government could not accept this amendment. All these men would go through medical examinations, and their duties would depend on their medical grades. Mr. MAXTON'S amendment was withdrawn.

Sir HERBERT WILLIAMS moved an amendment to the clause dealing with persons sentenced for failure to attend medical examination. He proposed that where a person supplied a certificate of permanent ill-health and the attendance at the prescribed place would be detrimental to his health, the medical examination should take place at his home. He suggested that in such cases the man's doctor should send a certificate. Mr. BEVIN said he could not accept the amendment. At present if a person supplied a medical certificate that he was suffering from ill-health and that attendance for medical examination at the prescribed place would be detrimental to his health, that certificate was put before the chairman of the medical board, who might direct that the person should not be summoned to attend unless and until he was fit to go. As the medical board consisted of medical men the Ministry took their advice and acted on it. That was a reasonable precaution against injustice.

The amendment was withdrawn. The Committee stage was completed and the Bill was read a third time.

Having passed through all its stages in the House of Lords, the Bill received the Royal Assent on December 18.

Provision of Wartime Nurseries

On December 9 in the House of Lords Lord NATHAN called attention to the importance of providing an adequate number of wartime nurseries, especially in view of the large number of married women who would be directed into industry. He said that these nurseries must be provided not in hundreds but in thousands. He believed that 200,000 children at least would have to be provided for in such nurseries after every other resource had been exhausted. The Government's own figure for the average number of children in wartime nurseries was forty, which meant that 5,000 nurseries would have to be provided, as against the 500 now contemplated. There would have to be accommodation for the whole twenty-four hours for children whose mothers would work at night.

Lord SNELL said it was impossible to estimate the extent to which women's labour would be drawn upon, but the urgency appeared to be in those key industrial districts which might call for quite rapid development, and that included all the services for child welfare. The Government would have first to observe the rate of intake into industry and then try to provide for nurseries in sufficient numbers in accordance with that intake. It would be unwise to fix in advance any number, which would depend on the rate of intake and the efficacy of any alternative methods that might be tried. Instructions had been given to local authorities designed to ensure adequate preparation for the expected need and to be ready for quick development. The three Departments concerned—the Ministry of Health, the Ministry of Labour, and the Board of Education—were collaborating closely with a view to adequate treatment of this difficult and urgent subject, as were maternity and child welfare authorities and local education authorities.

At the end of November 194 nurseries were in operation, and 209 were approved but not yet in full operation, providing for something over 15,000 children. There were in active preparation a further 264, and the Government felt, with their present knowledge of the need, that this programme was, on the whole, a fairly satisfactory one. Of 125 nurseries approved in November, 33 were allocated to the Midland area based on Birmingham, 20 to the industrial districts of Lancashire, and 17 to the outer districts of London. A suitable staff must include a number of trained nurses, supported by a large number of girls and women for general purposes, and a scheme of training for such supplementary labour had been worked out. Special arrangements had been made to meet the need for equipment. A list of articles had been prepared, and orders for them had already been placed.

Leprosy in British West Indies

Mr. GEORGE HALL furnished Dr. Morgan on December 10 with the following table setting out the incidence of leprosy in the British West Indies:

Colony		New Cases	Total Cases	Population
Bahamas	1940	3	17	70,332
Barbados	1939	5	63	193,082
Jamaica	1939	Not stated	249	1,195,465
Turks and Caicos	1938	2	5	5,300
Antigua	1940	Not stated	6	36,073
St. Kitts	1939	3	59	37,994
Montserrat	1939	Not stated	Not stated	13,541
Virgin Islands	1940	Not stated	Not stated	6,135
Trinidad and Tobago	1939	77	377	473,455
St. Lucia	1939	5	29	69,737
St. Vincent	1940	Nil	18	61,421
Grenada	1939	Nil	12	90,085
Dominica	1940	3	17	52,738
Bermuda	—	Nil	Nil	30,814
British Guiana	1939	45	565	341,237
British Honduras	—	Not stated	Not stated	57,767

Mr. Hall added that Dr. Muir, medical secretary of the British Empire Leprosy Relief Association, was in Trinidad holding a temporary appointment as medical superintendent of the Leper Colony, and proposed during his stay to undertake a leprosy survey in the West Indian area. The matter was receiving the attention of the Comptroller for Development and Welfare in the West Indies, and measures were being taken to deal with this disease in all the Colonies concerned.

Medical Certificates

Answering Mr. Rostron Duckworth on December 10, Mr. ERNEST BROWN said he had been asked by the British Medical Association to consider, in consultation with other Government Departments, whether steps could be taken to reduce the demands made on the medical profession for certificates in connexion with war activities. A conference took place between representatives of the Departments and of the Association, at which the whole matter was explored. The matter was now being considered by the Departments individually with the object of reducing to a minimum the number of purposes for which medical certificates were to be required.

Committee on Nurses' Salaries

Mr. ERNEST BROWN, replying on December 11 to Miss Lloyd George, said the committee on the salaries of nurses had held its first meeting on November 27. He intended that in regard to sanatoria and tuberculosis hospitals the committee's scope should extend to nurses possessing or in training for the certificate of the Tuberculosis Association, and that it should also extend to health visitors. Before the scope was so extended some adjustments in the committee might be necessary; and he was consulting the appropriate associations. Mr. Brown added that he had decided to set up a separate committee to draw up agreed scales of salaries for midwives on a national basis. He was consulting the appropriate associations of employers and workers. Lord Rushcliffe was ready to act as chairman of the committee for midwives as well as that for nurses. Some nurses' and midwives' posts involved the practice of both nursing and midwifery, and Mr. Brown would request the committees to consult together before making recommendations in overlapping matters of that kind. Mr. Brown asked for further notice before answering whether the committee would consider residence, uniform, and superannuation.

Rest and Feeding Centres.—Miss HORSBRUGH stated, in reply to a question on December 9, that no general standard had been laid down for the amount of accommodation, including feeding facilities, to be provided in rest centres. This had to depend in each area on a combination of widely varying local conditions, and it had been left to each rest centre authority to decide, in consultation with the Department's Senior Regional Officer, what was necessary for its own area. As a rough guide, however, it had been suggested that rest centre accommodation should be provided in target towns and their suburbs for not less than 8% of the population.

No. 49

INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended December 6.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for : (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for : (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases ; a blank space denotes disease not notifiable or no return available.

Disease	1941					1940 (Corresponding Week)				
	(a)	(b)	(c)	(d)	(e)	(a)	(b)	(c)	(d)	(e)
Cerebrospinal fever	132	7	30	4	2	144	3	36	6	5
Deaths		—	3				3	5		
Diphtheria	1,103	54	313	30	37	1,424	64	542	34	34
Deaths	27	1	9	2	—	35	—	11	—	1
Dysentery	165	3	73	—	—	92	2	50	—	—
Deaths			—	2	—			1	—	—
Encephalitis lethargica, acute	3	—	1	—	—	1	—	1	—	—
Deaths		—	—				2	—		
Enteric (typhoid and paratyphoid) fever						23	1	5	9	1
Deaths						—	—	—	—	—
Erysipelas		—	52	8	6		24	61	6	3
Deaths		1	—				—	1		
Infective enteritis or diarrhoea under 2 years										
Deaths	28	1	15	2	3	41	1	9	6	3
Measles	667	55	27	75	4	14,147	325	397*	—	9
Deaths	1	—	1	—	—	12	1	2	3	—
Ophthalmia neonatorum	83	2	14		2	80	—	9		—
Deaths										
Paratyphoid fever	8	—	3	—						
Deaths	—	—		—						
Pneumonia, influenzal†	979	52	13	3	13	782	37	12	—	10
Deaths (from influenza)	29	1	1	—	1	42	8	3	1	—
Pneumonia, primary			208	18				205	12	
Deaths		83		11	5		50		17	8
Polio-encephalitis, acute	—	—				2	—			
Deaths		—					—			
Poliomyelitis, acute	14	—	1	2	—	18	—	2	—	—
Deaths		—	—				—	—		
Puerperal fever		—	10	2	—	2	2	17	2	—
Deaths		—					1‡			
Puerperal pyrexia	178	5	9		5	109	3	22		—
Deaths										
Relapsing fever	—	—				—	—			—
Deaths										
Scarlet fever	1,324	35	238	59	35	1,597	69	231	62	58
Deaths	—	—	—	—	—	1	—	—	—	—
Small-pox	—	—	—		—	—	—	—		—
Deaths		—	—	—	—		—	—	—	—
Typhoid fever§	17	4	—	9	5					
Deaths	1	—								
Typhus fever	—	—	—	—	—	—	—	—	—	—
Deaths			—	—	—			—	—	—
Whooping-cough	1,725	209	52	48	19	2,421	17	226	—	23
Deaths	6	1	—	—	—	13	9	2	—	1
Deaths (0–1 year)	322	33	75	24	18	340	22	73	38	17
Infant mortality rate (per 1,000 live births)										
Deaths (excluding still-births)	4,271	552	592	184	114	5,979	908	646	205	132
Annual death rate (per 1,000 persons living)			12·9	12·2	¶			13·1	13·7	11·6
Live births	4,674	413	710	337	198	4,484	334	742	322	174
Annual rate per 1,000 persons living			14·4	22·4	¶			15·0	21·5	15·2
Stillbirths	177	14	24			159	7	26		
Rate per 1,000 total births (including stillborn)			33					34		

* In certain administrative areas only.

† Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

‡ Death from puerperal sepsis ?

§ Includes paratyphoid A and B for Northern Ireland.

¶ Owing to evacuation schemes and other movements of population, birth and death rates for Northern Ireland are no longer available.

EPIDEMIOLOGICAL NOTES

Discussion of Table

The feature of the returns for England and Wales during the week under review was the very large decrease in the notification of infectious diseases when compared with the preceding week. The largest decreases were those of scarlet fever 91, whooping-cough 234, measles 183, pneumonia 122, and dysentery 32. An increased incidence was recorded for diphtheria 56, puerperal pyrexia 54, and typhoid 10, these increases being due mainly to isolated and widely distributed cases. The only notable local rise was in Yorkshire, West Riding, where diphtheria was 31 cases in excess of the preceding week, due to the experience of the rural districts. The largest fall in the notifications of pneumonia occurred in Lancashire and Yorkshire, West Riding, where the totals were 38 and 48 below last week's figure. The most obvious deviations in the trend of scarlet fever were those of Lancashire, with 32 cases in defect, and Worcestershire, with 20 cases in excess, of the preceding week. The numbers of cases of measles in Staffordshire, Kent, and Herefordshire were 51, 27, and 39 below the totals of the previous week, but in Surrey, Reigate M.B., and Middlesex, Hendon M.B., there were increases of 37 and 21. The decreased incidence of whooping-cough was largest in Middlesex 52, Staffordshire 27, and Yorkshire, North Riding, 27, but—mainly because of outbreaks in Bognor Regis U.D. and Chichester R.D.—there was an increase of 35 cases in Sussex West.

A general decrease in the notifications of infectious diseases was also recorded in Scotland, although there was a relatively large increase, 19 cases, for dysentery.

The 75 cases of measles reported in Eire were an increase of 48 on the total of the previous week. Almost 90% of the cases were reported from two areas—Dublin 35 cases (an increase of 18) and Ballinasloe U.D., Co. Galway, 29 cases.

Dysentery

165 cases, a decrease of 32, were reported in England and Wales. Fresh outbreaks occurred in Nottinghamshire, East Retford R.D., 38 cases, and in Denbighshire, Denbigh M.B., 10 cases. Most of the remaining cases were recorded in Nottingham 38, Surrey 22, Lancashire 20, and Northumberland 10.

The chief centres of infection in Scotland were Renfrew County 11, Aberdeen County 15, and the burghs of Edinburgh 10 and Glasgow 15.

Quarterly Return of the Registrar-General for Scotland

The return for the September quarter of 1941 shows that on the whole Scotland enjoyed favourable health during this period. The civilian death rate was 11.6 per 1,000. The birth rate was 17.5 per 1,000—the highest recorded for any third quarter since 1932. Stillbirths registered during the quarter were equivalent to a rate of 37 per 1,000 total births and was the lowest recorded figure in Scotland for any quarter since registration began in 1939. The infant mortality rate of 63 per 1,000 live births was the highest rate since the third quarter of 1936, and was 6 higher than the rate for the corresponding quarter of 1940 and 4 above the average of the five years 1936-40. Maternal mortality of 4.8 per 1,000 live births was 0.1 below the average for the corresponding quarters of the five preceding years.

The death rate from all forms of tuberculosis was 73, and from respiratory tuberculosis 52 per 100,000. Compared with the average of the five preceding years these rates showed increases of 10 and 6 respectively.

254 deaths were attributed to the principal epidemic diseases ; this total was 163 fewer than in the third quarter of 1940. The chief causes of death were diphtheria 88, whooping-cough 83, and cerebrospinal fever 38.

Quarterly Return of the Registrar-General for Northern Ireland

The births registered during the third quarter of 1941 represented a rate of 22.0 per 1,000, this rate being 2.5 above the rate for the September quarter of 1940 and 2.0 above the average of the corresponding quarters of the five years 1936-40.

The death rate of 11.6 per 1,000 was the same as the rate for the third quarter of 1940 and was 0.2 above the average for the five preceding third quarters. Infant mortality was 66 per 1,000 births registered, compared with a rate of 76 for the corresponding quarter of the previous year and an average of 61 for the corresponding quarters of the five preceding years.

Twenty-eight deaths were recorded from whooping-cough—3 above the five-year average for the third quarters, and the 30 deaths from diphtheria were 10 above the average. Deaths from pulmonary tuberculosis numbered 235, compared with an average of 197 for the five preceding third quarters.

Medical News

An open conference on the general topic of "Science and the War Effort" has been arranged by the Association of Scientific Workers and will be held in the Caxton Hall, Westminster, S.W., on Saturday and Sunday, January 10 and 11, 1942. The subjects to be discussed include university training of scientists and training of technical personnel; building, housing, and A.R.P.; food and agriculture; application of scientific knowledge to problems of industrial production and to Services problems, including consideration of industrial health and conditions of work. Those who wish to take part should communicate at once with the conference secretaries, Association of Scientific Workers, 30, Bedford Row, W.C.1 (telephone: Chancery 5201).

Recent events in the Far East lend a grim interest to the report of the Director of Medical Services for Hong Kong for 1940. Dr. P. S. Selwyn-Clarke, in his section on the Civilian Medical (Defence) Scheme, writes that considerable time was spent in bringing up to concert-pitch the auxiliary medical services, such as first-aid posts, casualty clearing hospitals, relief hospitals, etc., for which doctors, sisters, nurses, dispensers, dressers, were trained so as to be available in the event of hostilities breaking out locally. One of the major difficulties was the recruiting of auxiliaries for emergency work, and this was accentuated by the shortage of nurses, due among other things to the compulsory evacuation. The St. John Ambulance personnel, about 1,500 in number, for the manning of first-aid posts in emergency, also had intensive training. The health division of the medical department was reorganized during the year, and the health inspectors worked, for the first time in the history of the Colony, under the direct control of health officers instead of under lay authorities.

At the last council meeting of the Queen's Institute of District Nursing, with Sir William Hale-White, M.D., in the chair, it was announced that the British War Relief Society of the U.S.A. had made a grant of £2,000 to help nursing associations in coastal areas which had suffered from air raids. A gift of £1,200 had also been received through the same benevolent agency from Miss Moule, an American nurse, and a group of her friends, who asked that the money might be sent to the Queen's Institute to help the nurses. During the past year £2,981 was received from the National Gardens Scheme.

Dr. Morris Fishbein, Editor of the *Journal of the American Medical Association*, has joined the British American Ambulance Corps' committee in Chicago.

To commemorate the missionary work of Sir Wilfred Grenfell, M.D., F.R.C.S., in Labrador a special 5-cent postage stamp will be issued in the near future by the Post Office Department of Newfoundland.

A department of nutrition has been established at McGill University, Montreal, in charge of Dr. E. W. Crampton, assistant professor of animal nutrition at Macdonald College.

Sir Henry Morris-Jones, M.D., Liberal M.P. for Denbigh, has been appointed chairman of the Welsh Parliamentary Party.

Major Percy Cecil Parker Ingram, M.B., has been appointed a Deputy-Lieutenant for the County of Monmouth.

General Smuts has lent his support to a campaign launched by South African friends of the Soviet Union for the provision of medical aid for Russia.

Letters, Notes, and Answers

All communications in regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, W.C.1.

ORIGINAL ARTICLES and LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS of their articles should communicate with the Secretary, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors over-seas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

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TELEPHONE NO.—B.M.A. and *B.M.J.*: EUSTON 2111.

TELEGRAPHIC ADDRESSES.—EDITOR, *Aitiology Westcent, London;* SECRETARY, *Medisecra Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.

QUERIES AND ANSWERS

Test for Urease Activity

Dr. J. F. MURPHY writes: Could any reader give me a simple and reliable test for urease activity in blood-urea estimation?

Immunization against Diphtheria

Dr. G. BAYNTON FORGE (Handley, Salisbury) writes: The articles on combined passive and active immunization against diphtheria (November 22, p. 717, and November 29, p. 759) are interesting. I wish to know if the injection of antitoxic serum with the toxoid will prevent the production of diphtheria carriers as will toxoid alone. Is six weeks' isolation for carriers sufficient? It works in closed communities, but what if these cases mixed with the unimmunized population? I have known diphtheria carriers to convey fatal diphtheria at the expiration of twelve months. In France I treated a Belgian soldier who was well into his second year as a carrier, verified by guinea-pig tests, and I left him still a carrier, but I read in the *Journal* some five years later that such cases could be quickly cured by an autogenous vaccine. The 50% increase in notifications of diphtheria in Wales in the past three months and the decline of 50% in the south-western counties for the corresponding period require explanation of the dissimilar effects of immunization. There may be other outside causes which are disregarded. A leading authority in the North considers defective drains to have no effect in spreading diphtheria; others in the South consider festering house refuse to be quite above suspicion as productive of diphtheria. I disagree. I have met many cases which could only be attributed to these two causes.

Income Tax

Partnership Liability

"Y.Z." was in partnership with "X.," who left the practice and has not accounted for his share of the tax due for the last year of his partnership. He is abroad, and "Y. Z." is informed that he is liable for the whole tax.

*** In strict law this is apparently correct, as the assessment is presumably made on the firm and the partners are jointly and severally liable. In view of the hardship, however, arising in the circumstances mentioned by "Y. Z." we doubt whether the authorities would proceed to extreme measures, and advise "Y. Z." to put the facts before the Board of Inland Revenue and ask them to leave the matter in abeyance until "X." returns from service in the R.A.M.C. abroad and can be sued for his share.

LETTERS, NOTES, ETC.

Status of the Ship Surgeon

Dr. A. GARDNER writes: It has been pointed out to me by a colleague that my letter on the above subject (November 8, p. 671) is liable to be interpreted in a way that was not intended. If so, this is due to the fact that the letter as originally written was meant to cover points mentioned by two other correspondents on the subject. I should like to make it clear that, apart from the first three paragraphs, in which I am in agreement with Dr. James Prendergast, my letter is concerned with service at sea in normal times.

Over 30 members attended the annual general meeting of the Medical Golfing Society at the Langham Hotel, W., with Mr. Harold Chapple in the chair. The motion that the society should carry on as usual was carried with acclamation, though it was agreed to postpone competitions for the present.